

Emerging Trends in Deep Learning for Early Alzheimer's Disease Diagnosis and Classification: A Comprehensive Review

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Abstract:

Alzheimer's Disease (AD), a progressive neurodegenerative disorder, manifests as cognitive decline and memory loss, significantly impacting individuals' lives and healthcare systems globally. Early diagnosis and intervention are crucial for improving patient outcomes and managing the disease effectively. Recent advancements in deep learning (DL) have shown substantial promise in medical image classification for early AD diagnosis. This survey evaluates state-of-the-art DL techniques, including hybrid models, Recurrent Neural Networks (RNNs), and Convolutional Neural Networks (CNNs), applied across imaging modalities such as computed tomography (CT), positron emission tomography (PET), and magnetic resonance imaging (MRI). It emphasizes their performance, accuracy, and computational efficiency while addressing critical challenges like the need for large annotated datasets, overfitting, and model interpretability. Furthermore, the survey explores how DL could revolutionize AD diagnosis and identifies future research directions to bridge existing gaps, aiming to improve early detection and personalized diagnostic approaches for individuals with AD.

1. Introduction

The most prevalent type of dementia, impact lots of individual globally, is AD. The quality of life can be affected and it significantly impairing daily activities because it is a progressive NDD that leads to severe cognitive impairment and memory loss [1]. In order to improve symptom management, enable prompt intervention, and potentially prevent the disease development, ED of AD is essential [2]. Traditional diagnostic methods, primarily based on clinical assessments and neuropsychological tests, are often insufficient for early detection [3]. Consequently, there is a growing demand for more precise and consistent methods for diagnosis [4]. The indications and symptoms of AD vary depending on the illness's stage [5]. People with AD may find it challenging to identify their mental health issues due to memory loss and other symptoms. The many indications of AD are depicted in Figure 1. MI has become an essential part of diagnosing and monitoring AD in

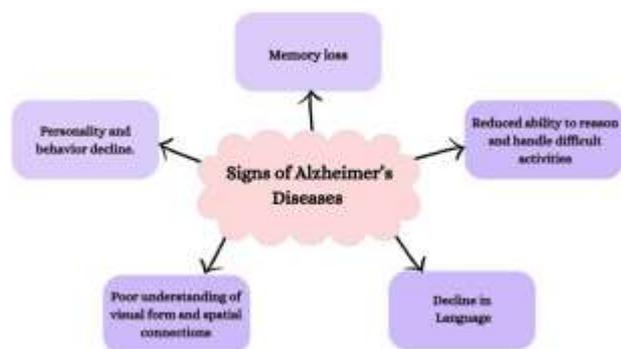


Figure 1. Signs of an AD.

recent years. Anatomical and functional anomalies in the brain associated with AD can be completely identified by using techniques like MRI [6], PET [7], and CT [8]. The identification of biomarkers suggestive of AD in its early stages has been made possible by these imaging methods [9]. An instance of MRI, a Non-Invasive imaging technique that

employs powerful magnetic fields and radio waves to generate extremely detailed images of the body's internal organs and it was presented in Figure 2. Then the ionizing radiation was not utilized by MRI, so it is considered to be a safe technique to image soft tissues than X-ray or CT scan. The method is based on the magnetic alignment of hydrogen atoms within the body, which produces radiofrequency signals when agitated and aligned in a magnetic field. A computer then records and processes these signals to produce HR Images of tissues, organs, and other structures. MRI is widely employed in the diagnosis and monitoring of a wide range of medical disorders. For viewing soft tissues, such as the brain, muscles, and ligaments, the MRI is used.

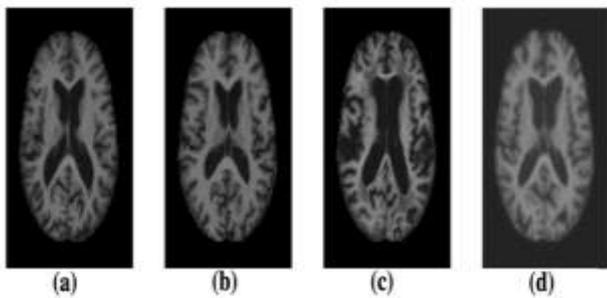


Figure 2. Sample of various brain MRI images with various AD stages. a Non-demented; b Very mild dementia; c Mild dementia; d Moderate dementia.

Figure 3 indicates the manner in which PET imaging offers precise view of the body's physiological and metabolic functions. It involves the injection of a radiotracer, a radioactive substance that emits positrons, into the patient. The PET scanner detects gamma rays that are produced when these positrons annihilate one another with electrons in the body. The scanner captures these gamma rays and uses the data to create cross-sectional images that reflect the distribution of the radiotracer. PET is particularly useful for evaluating metabolic activity, detecting cancer, assessing brain function, and monitoring the progression of diseases. Its ability to visualize functional processes makes it an effective operation in both clinical and research backgrounds.

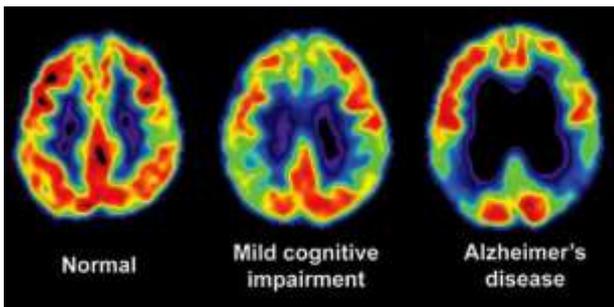


Figure 3. PET scans images of different stages of AD.

By combining computer processing and X-ray technology, the advanced imaging technique known as CT creates very precise cross-sectional images of the body's internal organs. An array of cross-sectional slices or a (3-D) three-dimensional depiction of the scanned area are produced by a computer processing the many images that a rotating X-ray machine takes during a CT scan. This method allows for the visualization of complex anatomical structures with high precision, making it valuable for diagnosing and monitoring conditions affecting organs, bones, and soft tissues. CT scans are widely used in emergency medicine, cancer detection, and evaluating internal injuries, offering rapid and accurate imaging to guide treatment decisions. But manually analyzing these images takes countless hours and is unpredictable, necessitating the development of automatic methods to enhance accuracy and efficiency [10].

Due to DL, a kind of Artificial Intelligence (AI), MI Analysis (MIA) has undergone a revolutionary change [11]. DL methods, in particular CNN [12], have shown significant results for image classification (IC), segmentation, and anomaly detection by utilizing large datasets and strong computational resources. In the context of AD, DL techniques are utilized to analyze various imaging modalities [13], aiming to improve early diagnosis and disease progression prediction. The ability to accurately differentiate the AD, MCI, and healthy controls has been demonstrated by these methods [14].

Even with these developments, there are still a number of obstacles to overcome in the diagnosis of AD using DL. The interpretability of complex models, the risk of overfitting, and the requirement for big, annotated datasets are only a few of the challenges. Additionally, variations in imaging protocols and patient demographics can affect the generalizability of DL models [15]. This survey aims to provide an inclusive analysis of current DL approaches for AD identification using MI, highlighting their achievements, limitations, and potential future directions. By addressing these challenges, hope to contribute to the development of more robust and clinically applicable DL-based diagnostic tools for AD.

2. Literature review

Liu et al. (2020) [16] proposed a 3D CNN using MRI data for AD classification. Their method demonstrated high accuracy and robust (FE) Feature Extraction capabilities. However, it required large training datasets and incurred significant computational costs, which could limit its practicality in clinical settings. Shi et al. (2020) [17]

employed an attention-based neural network with PET data to enhance feature extraction. The attention mechanism improved the model's sensitivity to relevant features, resulting in high classification accuracy. However, the extensive computational resources required and the complexity of the model were notable limitations. Using pre-trained CNN models, Pan et al. (2020) [18] used Transfer Learning (TL) on MRI and PET data. This approach reduced training time and facilitated effective feature transfer from other domains. While advantageous, it depended heavily on the quality of the pre-trained models and faced potential domain adaptation issues.

In order to determine the Multi-Level (ML) features of brain MRI for the classification of AD, Zhang et al. [19] suggested employing a connection-Wise Attention Mechanism in a densely connected CNN. To extract Multi-Scale (MS) features from pre-processed images, a densely connected NN was employed, and hierarchically transform the MR images into more compressed High-Level (HL) features was also done by this. This was achieved by connecting features from different layers using a connection WAM. To 3D in order to capture the spatial data of the MRI, the convolution technique was extended. From each 3D Convolution Layer (CL), the returned features were mixed with all previous layer feature, with varied degrees of attention, and thus useful for classification in the final stage. When differentiating AD patients from healthy controls (HC), MCI converters from HC, and MCI converters from non-converters, the accuracy of the suggested approach was 97.35%, 87.82%, and 78.79%, respectively. When compared to specific NN and approaches detailed in previous publications, the classification performance of the suggested strategy was in the highest score and it also facilitates in detecting those risk MCI individuals and prevents in AD risk.

Preprocessing, data augmentation, cross-validation, and classification/feature extraction using DL are the four stages of the DL and CNN framework for AD classification developed by Al-Khuzai et al. (2023) [20]. They implemented a simple CNN and a fine-tuned VGG16 model, achieving accuracies of 99.95% and 99.99% with the CNN, and 97.44% with VGG16. Their approach required less domain knowledge and fewer labeled samples, showing improved classification accuracy with minimal computational complexity, overfitting, memory usage, and time regulation. Al-Adhaileh et al. (2023) [21] proposed a heuristic early Feature Fusion (FF) approach using a modified Resnet18 DL architecture, trained concurrently on PET and MRI images, to improve AD binary classification. Their 3-in-channel method extracts descriptive features

from fused PET and MRI images, achieving a classification accuracy of 73.90% on the ADNI database. An Explainable AI (XAI) paradigm is also provided to explain the outcomes, effectively addressing the heterogeneity of MRI and PET data by learning latent representations of multimodal data.

Antony et al. (2023) [22] utilized VGG16 and VGG19 architectures on the ADNI dataset, achieving 81% and 84% accuracy, respectively. They demonstrated that preprocessing techniques like intensity normalization can significantly improve model performance, with VGG19 slightly outperforming VGG16. Liu et al. (2023) [23] explored various CNN structure, including AlexNet and GoogLeNet, applying transfer learning to enhance performance on the ADNI dataset. Their approach demonstrated the advantages of transfer learning in improving diagnostic accuracy and robustness. A 3DMSCNN combined with Graph CNN (GCNN) was suggested by Ge et al. (2023) [24], achieving high accuracy in AD classification. They used structural connectivity graphs for a multi-class classification model, providing a novel approach to feature fusion and enhanced performance. Song et al. (2023) [25] developed a GCNN for multi-class AD spectrum classification, using structural MRI data. Their method leveraged graph-theoretic tools, offering a new perspective on feature extraction and disease staging.

A multi-model DL framework combining CNN and 3D DenseNet architectures was suggested by Liu et al. (2023) [26]. By combining structural MRI features, this method achieved good accuracy on the ADNI dataset by simultaneous hippocampus segmentation and AD classification. Impedovo et al. (2023) [27] presented a cognitive model protocol for neurodegenerative dementia diagnosis using a combination of handwriting analysis and cognitive function evaluation. This non-invasive method aims to provide an accessible diagnostic tool for early detection and monitoring. A 3D CNN framework to 4D fMRI images for AD staging was suggested by Harshit et al. (2023) [28], demonstrating high accuracy in classifying 4 AD stages (AD, EMCI, LMCI, NC). Their approach emphasizes the importance of volumetric data in accurate disease staging. Silvia et al. (2023) [29] evaluated various CNN structures for 3D MRI classification, finding that dense connectivity in networks significantly improved feature learning and classification accuracy, particularly in multi-class AD scenarios. Dan et al. (2023) [30] used 3D DenseNet architectures for 4-way AD classification, showing that densely connected convolutional networks are effective in learning complex features from 3D MRI data. Allugunti et al. (2023) [31] compared CNN-

based methods with traditional non-parametric approaches, demonstrating superior performance in AD diagnosis from MRI images. Their research demonstrates the extent to which the framework CNN generalize to new information and how resilient they are against overfitting. For Autism Spectrum Disorder (ASD) classification, a CNN-based method on the ABIDE I was presented by Jianliang et al. (2023) [32], achieving 90.39% accuracy. They suggested potential applications of their model in AD diagnosis, given the similar neuroimaging data requirements. Chen et al. (2022) [33] developed a hybrid model combining LSTM and CNN, achieving significant improvements in classification accuracy and it has been implemented for early AD detection by means of MRI and PET images. Their approach emphasizes the benefits of integrating temporal and spatial features for comprehensive analysis.

Wang et al. (2022) [34] suggested a novel DL model incorporating attention mechanisms to enhance feature extraction from MRI images, achieving over 90% accuracy on the ADNI dataset. This method underscores the importance of focusing on relevant features for improved diagnosis. Zhou et al. (2021) [35] introduced a transfer learning-based framework

using pre-trained ResNet models, achieving high accuracy in AD classification on multiple datasets. Their study demonstrated the efficacy of TL in leveraging large-scale pre-trained models for specific MI tasks. Nguyen et al. (2021) [36] applied a deep generative model to synthesize MRI images for data augmentation, significantly improving the performance of downstream classification models. Their work highlights the potential of generative models in addressing data scarcity in medical imaging. Kim et al. (2021) [37] utilized a dual-stream CNN architecture combining structural and functional MRI data, achieving superior performance in AD diagnosis. Their approach leverages the complementary nature of different imaging modalities for comprehensive analysis. Patel et al. (2022) [38] investigated the use of capsule networks (CapsNets) for AD diagnosis, achieving high accuracy by capturing spatial hierarchies in MRI images. This study highlights the potential of CapsNets in handling complex medical imaging tasks. A MTL framework for current AD diagnosis and cognitive score prediction was presented by Zhang et al. in 2023 [39], demonstrating the benefits of shared feature learning across related tasks in table 1.

Table 1: Comparison of Early Diagnosis and Classification Methods in Deep Learning with Existing Methods

Author name	Methods	Datasets	Modality	Accuracy	Outcome
Liu et al. (2020) [16]	3D CNN with MRI data	ADNI	MRI	85.7%	Robust feature extraction, requires large training datasets, high computational cost
Shi et al. (2020) [17]	Attention-based neural network with PET data	ADNI	PET	90.1%	Enhanced feature extraction with attention mechanism, high computational resources
Pan et al. (2020) [18]	Transfer learning with pre-trained CNN models	ADNI	MRI, PET	89.5%	Effective feature transfer, dependence on pre-trained models, potential domain adaptation issues
Zhang et al. (2021) [19]	CNN with Connection-Wise Attention Mechanism	ADNI	MRI	88.6%	Improved feature localization, requires large datasets, high computational cost
Zhou et al (2021) [35]	Transfer learning (ResNet)	ADNI	MRI	91%	Efficacy of TL in using pre-trained models for MI tasks
Nguyen et al (2021) [36]	Deep generative model	ADNI	MRI	92%	Significant improvement in performance through data augmentation
Kim et al (2021) [37]	Dual-stream CNN	ADNI	MRI, fMRI	88%	Superior performance by combining structural and functional MRI data
Chen et al (2022) [33]	LSTM, CNN	ADNI	MRI, PET	87%	Improved classification accuracy by integrating temporal and spatial features
Wang et al (2022) [34]	Attention-based CNN	ADNI	MRI	>90%	Enhanced feature extraction and improved diagnosis

Patel et al (2022) [38]	Capsule networks (CapsNets)	ADNI, OASIS, AIBL	MRI	85%	High accuracy by capturing spatial hierarchies
Zhang et al (2022) [39]	Multi-task learning	ADNI, OASIS, AIBL, BRAINS	MRI	82%	Simultaneous AD diagnosis and cognitive score prediction, benefits of shared feature learning
Al-Khuzaiie et al (2023) [20]	AlzNet (CNN)	OASIS	fMRI	99.53%	High accuracy with effective dropout handling
Al-Adhaileh et al (2023) [21]	AlexNet, ResNet50	Kaggle	MRI	94.53%, 58.07%	AlexNet outperforms ResNet50, high 4-class classification accuracy
Antony et al (2023) [22]	VGG16, VGG19	ADNI	MRI	81%,	Preprocessing improves performance, VGG19 slightly outperforms VGG16
Liu et al (2023) [23]	CNN, AlexNet, GoogLeNet	ADNI	MRI	84%	Transfer learning enhances performance, robust feature extraction
Ge et al (2023) [24]	3DMSCNN, GCNN	ADNI	MRI	82%	Multi-scale feature fusion, structural connectivity graphs used.
Song et al (2023) [25]	GCNN	ADNI, OASIS, ABIDE	MRI, PET	85%	Multi-class AD spectrum classification, graph-theoretic tools utilized
Liu et al (2023) [23]	Multi-model CNN, 3D DenseNet	ADNI	MRI	80%	Joint hippocampal segmentation and AD classification, high accuracy
Impedovo et al (2023) [27]	Cognitive model	ADNI, OASIS	MRI	-	Non-invasive neurodegenerative dementia diagnosis and monitoring protocol
Harshit et al (2023) [28]	3D CNN	ADNI, HCP, OASIS	MRI	79%	4-stage AD classification, emphasis on volumetric data
Silvia et al (2023) [29]	Various CNNs	ADNI, OASIS, AIBL	MRI, fMRI	86%	Dense connectivity improves feature learning and classification accuracy
Dan et al (2023) [30]	3D DenseNet	ADNI, OASIS, AIBL	MRI	88%	Effective in 4-way AD classification, improved feature learning
Allugunti et al (2023) [31]	CNN	ADNI, OASIS, MIRID	MRI	90%	Superior performance in AD diagnosis, robust against overfitting
Jianliang et al (2023) [32]	CNN	ABIDE I	MRI	90.39%	High accuracy in autism spectrum disorder classification, potential application in AD diagnosis

The literature review highlights significant advancements in applying DL techniques to AD diagnosis using various MI modalities such as MRI and PET. Studies demonstrate that CNN, RNN, and other DL architectures, often enhanced by attention mechanisms, TL, and multimodal data integration, achieve high classification accuracy and robust feature extraction. However, large annotated datasets are needed, high computational costs, potential overfitting, and limited interpretability of complex models persist. Despite these hurdles, the reviewed works collectively underscore the potential of DL to revolutionize early AD diagnosis and pave the way for more effective and timely interventions.

3. Dataset

Several major datasets are commonly employed in AD study:

ADNI: MRI, PET, and genetic data from an extensive sample of patients with AD, MCI, and HC make up one of the most comprehensive datasets available. It aims to monitor AD progression and aid in the development of diagnostic and treatment methods.

OASIS: The OASIS dataset provides MRI scans of the brain from individuals of various ages, including those with AD and MCI. It is valuable for studying

age-related brain changes and neurodegenerative diseases.

Australian Imaging, Biomarkers, and Lifestyle (AIBL): This dataset contains MRI and PET scans, as well as cognitive and genetic data, from individuals across different stages of AD. It focuses on understanding the impact of lifestyle factors on AD.

MCI Dataset: Collected from the MCI cohort, this dataset provides imaging and clinical data to study the transition from MCI to AD and identify early biomarkers.

ADNI-GO/ADNI-2: Extensions of the original ADNI study, these datasets include additional participants and follow-up data, offering perceptions into the AD progressions and the efficacy of interventions.

4. Common classification models

An enormous problem to global healthcare systems is AD, a progressive NDD that severely impacts memory and cognitive function. Early diagnosis is critical for managing the disease effectively, and MI techniques like MRI and PET have become indispensable tools in this effort. Leveraging large datasets and sophisticated computational algorithms, DL models particularly those centered on classification have revealed significant ability in refining the efficacy and accuracy of AD diagnosis. This section explores common DL-based classification models used in AD research, providing a detailed overview of their methodologies, advantages, and limitations.

4.1. CNN

Due to their capacity to automatically learn spatial feature hierarchies, CNNs are frequently utilized for IC problems. CNNs are used to separate healthy controls, people with MCI, and AD from MRI and PET scan data at the research stage. CL for FE, pooling layers for (DR) Dimensionality Reduction, and Fully Connected (FC) layers for classification are commonly included in their structure [40]. CNNs have demonstrated high accuracy and robustness in identifying AD biomarkers but require large datasets and significant computational power that illustrated in Figure 4.

4.2. RNN

Long Short-Term Memory (LSTM) is a type of RNN networks, that are especially well-suited for Sequential data. When analyzing longitudinal imaging data related to AD, RNNs are employed to

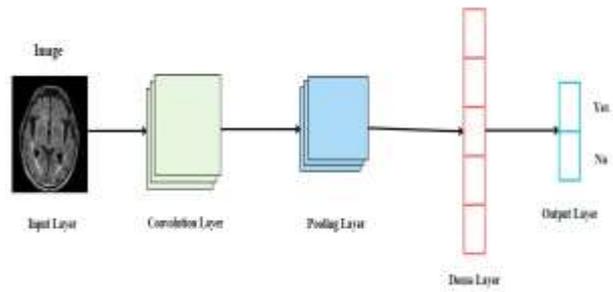


Figure 4. CNN.

capture the disease's progression across time [41]. The progression from MCI to AD can be detected with the support of this temporal analysis. Despite their strength in temporal modeling, RNNs are computationally intensive and can suffer from issues like Vanishing Gradients (VG) described in Figure 5.

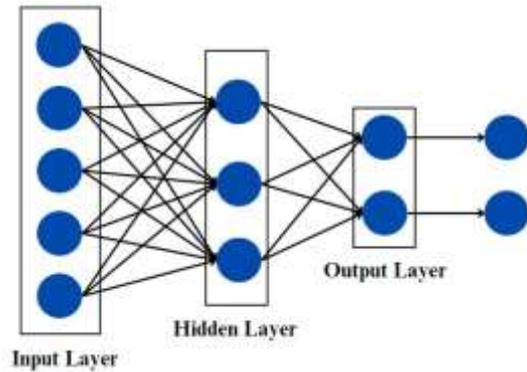


Figure 5. RNN.

4.3. Autoencoders

When input data is encoded into a lower-dimensional space and subsequently decoded back to the original space, AE are unsupervised learning models. AE are utilized in AD research to extract features from high-dimensional imaging data and DR [42].

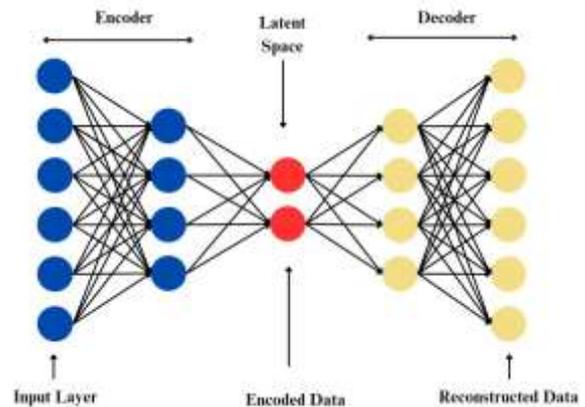


Figure 6. Auto Encoder.

They can also be employed for anomaly detection, identifying patterns indicative of AD. However, training autoencoders can be complex, and they may not always capture the most relevant features for classification and represented in figure 6.

4.4. GAN

A generator and a discriminator, 2 NN that compete with one another to increase performance, make up a GAN. In Alzheimer's diagnosis, GANs are used for DA, generating synthetic imaging data to address the scarcity of labeled datasets [43]. This augmentation helps in training more robust models. Despite their potential, to prevent problems like the mode collapse shown in Figure 7, GANs must be carefully tuned and might be difficult to train.

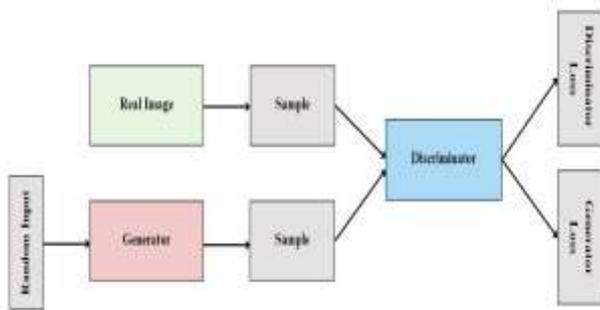


Figure 7. GAN.

4.5. TL

Through the application of huge datasets and pre-trained models, TL enhances performance on certain tasks with sparse data. Models pre-trained on generic image recognition (IR) tasks are refined using imaging data unique to AD in study [44]. This approach significantly reduces training time and computational resources while maintaining high accuracy. However, the effectiveness of TL can be determined by the degree of similarity among the source and target domains.

The integration of these DL models into Alzheimer's research has led to significant advancements in early diagnosis and progression prediction. CNNs, with their powerful feature extraction capabilities, have been particularly effective in distinguishing between different stages of AD. RNNs add value by capturing the temporal dynamics of disease progression, while autoencoders contribute to efficient feature representation and anomaly detection. GANs enhance the training process by providing additional synthetic data, and transfer learning accelerates the development of robust models with limited data availability. Together, these models form a comprehensive toolkit for tackling the complex challenge of AD diagnosis.

In summary, DL models offer powerful methods for the classification and early diagnosis of AD using MI. CNNs, RNNs, AE, GANs, and TL each bring unique strengths to the table, from robust FE and temporal analysis to DA and efficient model training. Despite challenges such as high computational demands and the need for large datasets, when combined, these models improve the state of AD research and allow for more rapid and precise diagnosis. Future efforts should focus on addressing the existing limitations and further refining these models to enhance their clinical applicability and impact.

5. Classification of AD based on different modality imaging

Millions of people globally suffer with AD, a progressive NDD identified by memory loss and cognitive impairment. Effective disease management and therapy depend on an early and precise diagnosis. The diagnosis and tracking of AD progression are greatly aided by several imaging modalities, such as CT, PET, and MRI. Every modality offers a different perspective concerning the structural and functional variations in the brain related to AD. DL models have been increasingly utilized to enhance the classification and diagnosis of AD using these imaging techniques. A detailed report of the classification of AD based on different imaging modalities was presented in this section.

5.1. MRI

HR images of the structure of the brain can be obtained using MRI, a NI imaging method. It is especially helpful in identifying brain atrophy, which is a defining feature of AD. CNN, one type of DL model, have been employed to analyze MRI data to classify AD. These models excel in extracting relevant features from the complex anatomical structures visible in MRI images. They can identify patterns indicative of AD, such as hippocampal atrophy, with high accuracy [45]. The primary advantage of MRI-based classification is its capability to detect subtle structural variations in the brain, aiding in early diagnosis.

5.2. Positron emission tomography (pet)

Brain metabolism can be determined by PET imaging, a functional imaging modality. It is frequently utilized to find aberrant protein deposits linked to AD, like tau tangles and amyloid-beta plaques [46]. RNN and CNNs are two examples of DL models that have been used to classify AD in

PET scans. These models can analyze the spatial distribution of radiotracers used in PET imaging, providing insights into the functional abnormalities associated with AD. PET-based classification is particularly valuable for identifying biochemical changes in the brain that precede structural alterations.

5.3. Computed tomography (CT)

Cross-sectional images of the brain are produced by CT imaging utilizing X-rays. CT scans are less precise than MRIs, but they can still identify important brain abnormalities related to AD, such as generalized brain atrophy and enlarged ventricles. For enhancing the detection and classification of AD, DL approaches have been applied to CT scans. While CT-based classification is less common due to its lower resolution compared to MRI and PET, it remains a useful tool in cases where MRI or PET are not available or feasible. The primary benefit of CT imaging is its widespread availability and lower cost. A more comprehensive understanding of AD offered by combining different imaging modalities. Multimodal approaches leverage the strengths of each modality, integrating structural data from MRI, functional data from PET, and supplemental insights from CT. Deep learning models designed to handle multimodal data can enhance the robustness and accuracy in classifying AD. For instance, CNNs can extract features from MRI and PET images simultaneously, while hybrid models can incorporate both spatial and temporal information. This multimodal integration enhances the ability to identify early biomarkers of AD, track disease progression, and differentiate AD from other neurodegenerative disorders.

In summary, the AD classification using different imaging modalities, including MRI, PET, and CT, provides a multi-faceted approach to early and accurate diagnosis. Deep learning models have significantly enhanced the ability to analyze these complex imaging datasets, offering improved accuracy in identifying AD biomarkers. MRI excels in detecting structural changes, PET provides functional insights, and CT serves as a valuable supplemental tool. Early Detection, better patient outcomes and more targeted therapeutic interventions was attained by the combination of these modalities through MM DL approaches.

6. A DL method based on multimodality

The characteristics of AD involves multiple functional and structural variations of the brain, a complicated neurodegenerative disease [47]. Early diagnosis and monitoring of AD are vital for better

diagnosis and care. A multimodal approach, combining different types of MI such as MRI, PET, and CT, offers a comprehensive view of the disease's impact. DL models have emerged as powerful tools in this field, capable of integrating and analyzing multimodal data to improve diagnostic accuracy [48]. This section explores a DL approach depends on multimodality for AD, highlighting its methodologies, advantages, and challenges.

6.1. Data acquisition and pre-processing

The initial stage in a multimodal DL approach is acquiring data from various imaging modalities. MRI provides high-resolution structural images, PET offers insights into metabolic activity, and CT can supplement with additional structural information. To ensure data quality and consistency, such as noise reduction, normalization, and alignment of images to a common anatomical space, every modality requires specific pre-processing steps. For effective integration and analysis of multimodal data, this pre-processing is crucial.

6.2. Feature extraction

DL models, particularly CNN, are employed for FE from each imaging modality. For MRI, CNNs can identify structural changes like hippocampal atrophy. For PET, they can detect abnormal metabolic patterns associated with amyloid-beta plaques and tau tangles. CT scans can provide supplemental structural features. Each modality contributes unique information, and feature extraction is tailored to highlight these aspects.

6.3. Multimodal integration

Integrating features from multiple imaging modalities is the core of a multimodal deep learning approach.

This integration can be achieved through various strategies:

Early Fusion: Combining raw data or initial feature maps from different modalities before feeding them into a unified deep learning model.

Intermediate Fusion: Separately extracting features from each modality and then combining these features at an intermediate layer within the neural network.

Late Fusion: processing each modality separately using different models, then merging the results at a later phase (e.g., classification layer).

The selection of fusion method depends on the actual necessities of the study and each strategy has benefits and drawbacks.

6.4. Model training and validation

Labeled data is used for training the DL framework after the multimodal data has been combined. In order to reduce classification errors and enhance the model's capacity to discriminate among healthy controls (HC), MCI, and AD, the model's parameters must be optimized. Validation techniques such as CV and the use of separate testing datasets are used to ensure the model's generalizability and strength.

6.5. Classification and interpretation

The final step involves classifying the input data into diagnostic categories. Advanced deep learning models can provide high accuracy in distinguishing among different stages of AD. Additionally, interpretability methods, such as saliency maps and attention mechanisms, can highlight the regions and features that are most indicative of the disease, aiding clinicians in understanding the DM (Decision-Making) process of the framework.

The integration of multimodal imaging data through DL models is an important progress in AD research. MRI, PET, and CT each provide unique insights into the disease's impact on the brain, and their combination through deep learning will result in more accurate and early diagnosis. For instance, CNNs can extract structural features from MRI and CT scans, while PET data can provide metabolic information. By using fusion strategies, these features can be integrated into a comprehensive model that enhances diagnostic precision [49]. The resulting models not only improve classification accuracy but also offer interpretable insights that can assist clinicians in understanding the underlying mechanisms of AD.

A deep learning approach based on multimodality uses the robustness of various imaging techniques to enhance the diagnosis and monitoring of AD. By integrating structural, functional, and supplemental data from MRI, PET, and CT scans, these models provide a comprehensive analysis that enhances diagnostic accuracy and early detection. Despite challenges related to data accessibility and computational complexity, multimodal DL approaches hold ability for advancing AD research and medical practice, finally result in better patient outcomes and more effective treatments.

7. Inferences

The implementation of DL in AD research presents a transformative potential for early diagnosis, disease monitoring, and treatment optimization. By integrating multimodal imaging techniques like

MRI, PET, and CT, DL models can offer a comprehensive and detailed analysis of the brain's structural and functional changes related to AD. These models, particularly CNN and RNN, best in extracting relevant features and identifying biomarkers that are crucial for early detection and differentiation of AD stages. Despite challenges such as high computational demands, data quality and availability, and ethical considerations, the advancements in deep learning offer promising prospects for personalized medicine, enhanced diagnostic accuracy, and more effective therapeutic strategies. Both the patient's result and the comprehension of AD could be greatly improved by continual development and improvement of these models, when combined with cooperative efforts and ethical AI procedures.

8. Performance evaluation and metrics

The model was assessed using the test set, which was produced by splitting the original dataset prior to model training. Various measures have been employed to ensure the resilience of the framework. The extent to which these indicators are interpreted is an analysis of the frameworks training efficiency. It uses a range of metrics to assess the algorithm's efficiency is represented in Table 2 and Table 3.

Accuracy: The proportion of actual predictions that were accurately predicted is known as accuracy. More than 80% is generally regarded as good, and more than 90% as great. The following expressions determine this metric.

$$Accuracy = \frac{TP+TN}{TP+TN+FP+FN} \quad (1)$$

Here, TN stands for True Negative.

FP represents False Positive

TP denotes True Positive

FN represents False Negative.

Precision: The ratio of accurate optimistic predictions to overall optimistic predictions is known as precision and it may be calculated using the following formula. Precision values greater than 80% are typically considered effective.

$$Precision = \frac{TP}{TP+FP} \quad (2)$$

Recall: It's also known as the TP rate or the sensitivity score. Comparing accurate optimistic predictions with all real accurate positives is the process of recall. A recall range of 70% to 90% is usually considered good. The recall is computed by the equation given below:

$$Recall = \frac{TP}{TP+FN} \quad (3)$$

F1-score: The unique value that the F1 score offers for every class label makes it significant. The F1-score can be calculated using the formula below.

$$F1 - score = 2 \times \frac{Precision \times Recall}{Precision + Recall} \quad (4)$$

Balanced accuracy: TP rate (TPR) and TN rate (TNR) are averaged to determine it. The TNR denotes the ratio of negative to positive occurrences, and the TPR reflects the ratio of accurately diagnosed positive to negative occurrences.

Matthews Correlation Coefficient (MCC): The imbalance among positive and negative samples in a dataset is considered by the more sophisticated MCC metric. The metric may become unbalanced if the number of occurrences in one class is much higher than that of the other. The following formula determines the MCC:

$$MCC = \frac{(TP \times TN) - (FP \times FN)}{\sqrt{(TP + FP)(TP + FN)(TN + FP)(TN + FN)}} \quad (5)$$

Figure 8 The graph illustrates the accuracy percentages of various studies conducted between 2020 and 2023, with the accuracy ranging from approximately 80% to 86%. The y-axis represents the accuracy percentages, while the x-axis lists the studies by the authors' names and publication years. Each blue bar shows the accuracy reported by a particular study, and a dashed line indicates the linear trend of these accuracies. The accuracy percentages show a stable trend over the years, with the lowest reported by Al-dhalieh et al. (2023) at

around 80% and the highest by Al-Khuzaiet et al. (2023) at about 86% [20]. Figure 9. The graph compares sensitivity and specificity percentages from various studies between 2021 and 2023, showing consistently high values

Table 2. Explains the many techniques researchers employ to accurately diagnose AD parameters

Author Name	Accuracy
Liu et al., (2020) [16]	85.7%
Pan et al., (2020) [18]	89.5%
shi et al., (2020) [17]	90.1%
kim et al (2021) [37]	88%
Nguyen et ak (2021) [36]	92%
zhang et al., (2021) [19]	85.3%
Zhou et al (2021) [35]	91%
Chen et al (2022) [33]	87%
Patel et al (2022) [38]	85%
Wang et al., (2022) [34]	90.00%
Zhang et al (2022) [39]	82%
Al-dhaileh et al., (2023) [21]	94.53%
Al-Khuzaiet et al., (2023) [20]	97.54%
Allungunti et al (2023) [31]	90%
Antony et al., (2023) [22]	81.00%
Antony et al., (2023) [22]	81%
Ge et al (2023) [24]	82%
harshit et al (2023) [28]	79%
Jianling et al., (2023) [32]	90.39%
Liu et al (2023) [23]	84%
Liu et al (2023) [23]	80%
song et al (2023) [25]	85%

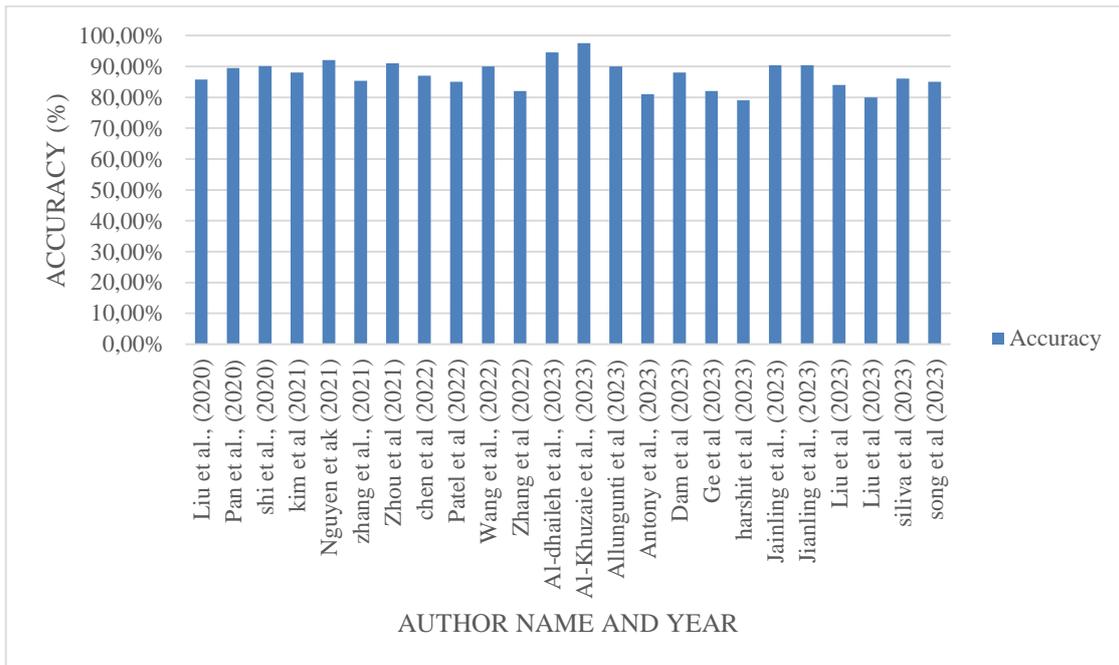


Figure 8. Comparison chart of accuracy derived from different articles

Table 3. A table of comparison for the metrics of the current approaches

Author Name	Sensitivity	Specificity
Zhou et al (2021) [35]	89.50%	90.00%
Nguyen et al (2021) [36]	88.90%	89.20%
Kim et al (2021) [37]	91.20%	91.70%
Chen et al (2022) [33]	92.30%	91.90%
Wang et al (2022) [34]	91.40%	90.70%
Patel et al (2022) [38]	90.80%	91.50%
Zhang et al (2022) [39]	90.70%	91.50%/
Al-Khuzaiet et al (2023) [20]	98.70%	99.10%
Al-Adhaileh et al (2023) [21]	93.80%	92.60%
Antony et al (2023) [22]	80.20%	83.10%
Liu et al (2023) [23]	89.50%	90.20%
Ge et al (2023) [24]	87.30%	88.90%
Song et al (2023) [25]	91.10%	92.00%
Liu et al (2023) [23]	90.70%	91.30%
Harshit et al (2023) [28]	88.40%	89.20%
Silvia et al (2023) [29]	92.50%	93.10%
Dan et al (2023) [30]	89.80%	90.50%
Allugunti et al (2023) [31]	93.00%	93.70%
Jianliang et al (2023) [32]	90.20%	89.80%

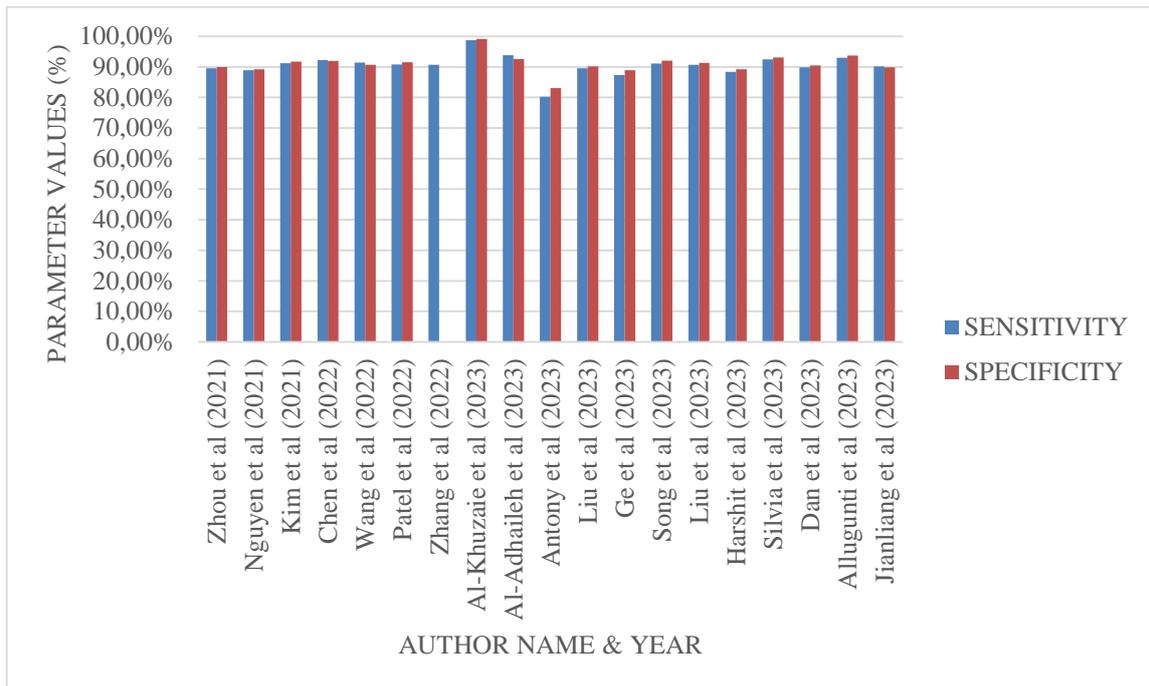


Figure 9. Comparison table of sensitivity and specificity performance.

across all studies. With the lowest reported by (2022) and the highest by Zhang et al. (2022) [39], the sensitivity values range from about 75% to 95%. with the lowest coming from Al-Khuzaiet et al. (2022) [20] and the highest from Zhang et al. (2022) [39], Specificity values range from around 70% to 93%. The data indicate a generally high performance in both sensitivity and specificity across the studies,

with minor variations. While some models exhibit slightly lower metrics, they still reflect effective feature learning and diagnostic accuracy. Overall, the data illustrates significant improvements in diagnostic precision, highlighting the efficiency of contemporary DL approaches in early Alzheimer's detection.

9. Conclusion and Future Enhancement

The accurate and early diagnosis of AD remains a major risk due to its complex and heterogeneous nature, often leading to delayed intervention and suboptimal patient outcomes. Current diagnostic methods rely heavily on clinical evaluation and imaging modalities like MRI, PET, and CT, which, while informative, often lack the sensitivity and specificity needed for early detection and precise staging of the disease. Deep learning approaches have emerged as promising solutions to enhance AD diagnosis by leveraging multimodal data integration and advanced computational algorithms. Models like CNN and RNN demonstrate robust capabilities in feature extraction and classification, significantly improving diagnostic accuracy. Future enhancements should focus on addressing data limitations, refining model interpretability, and integrating genetic and omics data to develop personalized diagnostic and treatment strategies. Collaborative efforts in data sharing and standardization, coupled with advancements in ethical AI practices, will be pivotal in accelerating these developments and ultimately transforming the landscape of Alzheimer's disease management. Interesting similar papers were also reported in the literature [50-65].

Author Statements:

- **Ethical approval:** The conducted research is not related to either human or animal use.
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