



Review Article

A systematic review on recent methods on deep learning for automatic detection of Alzheimer's disease

Radhakrishna Chamakuri^{*}, Hyma Janapana

Department of Computer Science Engineering, GITAM School of Technology, Visakhapatnam, Andhra Pradesh, 530045, India

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ABSTRACT

Alzheimer's disease (AD) is the most frequent cause of dementia, however, and it is caused by a number of different disorders. With regard to the elderly population all over the world, Alzheimer's disease is the seventh largest cause of mortality, disability, and reliance. Depression, social isolation, inactivity, alcohol, smoking, obesity, diabetes, high blood pressure, and age are all variables that can increase the likelihood of getting dementia. Other risk factors include social isolation, depression, and smoking. A diagnosis of Alzheimer's disease at an earlier stage may improve the odds of receiving care and therapy. Medical professionals often diagnose AD based on a limited number of symptoms. On the other hand, it is now possible to identify and categorize Alzheimer's disease (AD) because of technological advancements such as artificial intelligence (AI). However, to identify the current AI-enabled approaches, we must conduct an investigation into the state of the art. This breakthrough in diagnosis methodologies will enable the development of the Clinical Decision Support System (CDSS), capable of automatically diagnosing Alzheimer's disease (AD) without human expertise. In this publication, we conduct a systematic review of sixty research articles previously reviewed by other researchers. The systematic review sheds light on the synthesis of new knowledge and ideas. This study discusses the current approaches for machine learning, deep learning methods, ensemble models, transfer learning, and methods used for early Alzheimer's disease diagnosis. This paper provides answers to a large number of research issues and synthesizes fresh information that is helpful to the reader on many elements of AI-enabled approaches for Alzheimer's disease diagnosis. In addition, it has the potential to stimulate additional research into more effective methods of computer-based intelligent identification of Alzheimer's disease.

1. Introduction

Alzheimer's Disease (AD) is a brain disorder that gets worse over time. It's characterized by changes in the brain that lead to deposits of certain proteins. Alzheimer's disease causes the brain to shrink, and brain cells eventually die. Alzheimer's disease is the most common cause of dementia, causing a gradual decline in memory, thinking, behavior, and social skills. These changes affect a person's ability to function. According to the World Health Organization (WHO), dementia is an umbrella term for several diseases affecting memory, other cognitive abilities, and behavior that interfere significantly with a person's ability to maintain their activities of daily living. Although age is the strongest known risk factor for dementia, it is not a normal part of aging. Since AD is one of the causes of dementia, it is critical to detect it early; otherwise, it will worsen patients' situations over time. Alzheimer's disease is a slowly progressive brain-causing condition that affects memory, thinking, and

behavior. Unless treated in time, it is life-threatening and dangerous. Nevertheless, technological innovations like artificial intelligence (AI) and cloud computing enable unprecedented means of monitoring Alzheimer's patients. Deep learning methods have enhanced artificial neural networks to solve various types of problems. Deep learning models, in particular, mimic human brain processes in order to ascertain knowledge from training samples and detect diseases. Towards this end, many researchers contributed to the detection of AD using machine learning (ML) and deep learning (DL) methods. In this paper, we used a systematic review approach to review literature findings. Here is a summary of our contributions to this paper.

1. We employ a systematic review approach that utilizes a PRISMA model-based article selection process to diagnose AD using deep learning techniques.

^{*} Corresponding author.

E-mail address: radhakrishnach@gmail.com (R. Chamakuri).

2. Our findings shed light on various aspects of the learning-based techniques used for automatic AD diagnosis.
3. The most recent research articles revealed significant research gaps that led to particular conclusions.

The paper will be structured as follows in the subsequent sections: In the second section, we present our methodology for conducting a comprehensive review of DL algorithms for AD diagnosis. In Section 3, we perform a literature review and address the questions outlined in our methodology. Section 4 delineates the research gaps discovered in the survey, whilst Section 5 ends our study and provides recommendations for future research.

2. Material and methods

Our research specifically focuses on a thorough literature review that illuminates various deep learning methods for Alzheimer's disease detection. Various techniques for machine learning are among the components: deep learning methods, ensemble models, transfer learning, and methods used for early AD diagnosis. It also investigates various research questions posed for investigating AD diagnosis techniques.

2.1. Research questions

The objective of this paper's literature synthesis is to generate novel and valuable knowledge. This research examines the literature to deal with particular research concerns. These questions reveal invaluable information embedded in the aesthetic articles. The study we conduct includes recent advancements in the specified field.

- RQ1: What machine learning methods are used to diagnose AD?
 RQ2: What are the current deep learning techniques for diagnosing AD?
 RQ3: What are existing multi-model and multi-class classification techniques for AD detection?
 RQ4: What are the existing feature selection methods and hybrid approaches to AD diagnosis?
 RQ5: What are some of the existing approaches to deep learning using fMRI imagery?
 RQ6: What are the existing methods for focusing on early AD diagnosis using learning-based approaches?
 RQ7: What are the existing ensemble and transfer learning methods for automatic AD detection?
 RQ8: What are the current approaches to AD detection using 3D data?
 RQ9: Role of LLMs in AD detection.
 RQ10: What are the datasets used in the existing research for AD detection?
 RQ11: What are the widely used performance metrics for evaluating models in AD detection?
 RQ12: Recommendations to enhance the AD diagnosis using various techniques.

In order to acquire useful knowledge, these research questions investigate the existing literature. Reviewing the pertinent

literature allows us to provide answers to each question. Section 4.1 provides an overview of RQ1 and discusses machine learning models used for AD diagnosis. Section 4.2 addresses RQ2 by concentrating on the current deep learning techniques for AD detection. Section 4.3 sheds light on RQ3, providing an understanding of existing multi-model and multi-class classification techniques. Section 4.4 addresses RQ4, delving into various existing feature selection and hybrid techniques. Section 4.5 provides an answer to RQ5, which pertains to techniques utilizing FMRI. Section 4.6 addresses RQ6, delving into the techniques employed for early AD diagnosis. Section 4.7 answers RQ7, showing the existing transfer learning and ensemble learning methods. Sections 4.8 and 4.9 respectively address RQ8 and RQ9. Section 4.10 provides an answer to

RQ 10. Section 4.11 pertains to widely used performance metrics for evaluating models in AD detection to address the RQ11 and section 4.12 covers the RQ12.

2.2. The methodology of Research

According to the PRISMA model, which is a broadly utilized instrument that enhances the quality of articles in systematic reviews, our study approach and article assortment procedure are grounded on the PRISMA model. In the beginning, we managed to collect a total of 168 articles from a wide variety of trustworthy resources as well as the database maintained by Scopus. After that, we performed a filtering procedure on the articles, which included the application of eligibility and exclusion criteria, the removal of duplicates, and the elimination of items that were irrelevant. Finally, it came down to 104 research articles that could satisfy the selection process.

A methodical strategy is utilized in the article selection process, which is depicted in Fig. 1. This strategy is designed to improve the overall quality of the results obtained from research that involves a literature review.

2.3. Data sources

The collection of research articles is from reputable data sources, and we subjected them to peer assessment. Fig. 1 depicts the PRISMA methodology that governs the article section. We employ a systematic methodology in the article selection process. The following digital libraries are utilized for acquiring research articles:

Google Scholar (<https://scholar.google.com>)
 Springer (<https://www.springer.com/in>)
 Elsevier (<https://www.elsevier.com/en-in>)
 IEEE Xplore (<https://ieeexplore.ieee.org/Xplore/home.jsp>)
 Hindawi (<https://www.hindawi.com/>)
 MDPI (<https://www.mdpi.com/>)

2.4. Search process

Table 1 is a compilation of various phrases utilized in article searches. The research procedure uses electronic libraries and their related search software to group the most pertinent, peer-reviewed publications.

Using different phrases in the search process yields articles on various existing methods for diagnosing AD. A systematic evaluation of the publications cannot encompass all publications identified throughout the search procedure. Table 1 delineates the requisite parameters to improve the article selection procedure.

2.5. Criteria to improve article selection process

Finding and selecting excellent in quality research manuscripts suitable for a systemic assessment was made possible by using clearly stated criteria. To ensure that only relevant and trustworthy studies were included in the final choice, these criteria played a pivotal role.

Additionally, the filtering process prioritized the most recent articles, ensuring that the review remained up-to-date with the latest research developments.

2.6. Bibliographic Research results

The bibliographic findings from the research publications that were obtained throughout the selection process are presented in this part. A breakdown of the papers by publisher and year can be found in Table 2.

Table 2 illustrates the reduction from the initial collection of 165 articles to 101 articles during the screening, eligibility, and inclusion stages.

The yearly distribution of the published articles that were utilized in this overall methodical investigation evaluation is presented in Table 3.

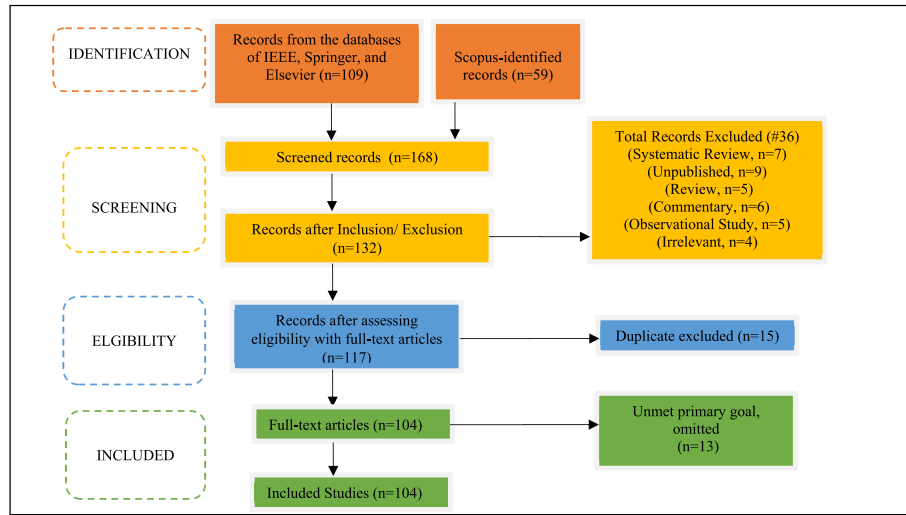


Fig. 1. A collection of articles using the PRISMA paradigm.

Table 1
Criteria utilized for article decision-making.

SL. No.	Inclusion Criteria	Exclusion Criteria	Justification
1	English	Other languages	The language most used worldwide is English.
2	ML practices for AD diagnosis	ML practices for other than AD diagnosis	Only ML practices that are specifically used for AD diagnosis are preferred
3	DL procedures for AD diagnosis	DL procedures for other than AD diagnosis	Preferred DL procedures are specifically used for AD diagnosis.
4	Ensemble methods for AD diagnosis	Ensemble learning methods for other than AD diagnosis	Ensemble learning techniques specially used for AD diagnosis are preferred
5	Early AD detection methods	Early detection methods for diseases other than AD	Early detection techniques specially used for AD diagnosis are preferred
6	Peer-reviewed	Unreviewed by experts in the field	Reviewed articles demonstrate high-quality research.

Table 2
Collection of articles from 2016 to 2024.

Stage	AD diagnosis research articles
Stage1	Screening: 132
Stage 2	Eligibility: 117
Stage3	Article Included (Categorization by year): 104
	Until 2016 2017–2019 2020–2024
	1 27 76

Table 3
Yearly published articles used for systematic review.

Year of publication	# Articles
2016	1
2017	2
2018	7
2019	18
2020	27
2021	21
2022	16
2023	10
2024	2

Although the study publications cover several years, we have opted to focus on the most recent period, with 97 % published between 2018 and 2023, to pinpoint the research gaps that will be addressed in the subsequent section.

Table 4 presents the distribution of journal articles and conference papers across various publishers. Elsevier, Springer, MDPI, and IEEE have published a significant number of articles, including those from IEEE conferences.

As presented in Fig. 2, the highest percentage of articles is 27 %, which is from the year 2020, and the least percentage is 1 % from 2016.

3. Results

In the following section, key research gaps in the existing literature are presented. It elucidates key research initiatives, including their methodologies, procedures, defined algorithms, and datasets that were utilized for empirical research, as well as the limitations of those research endeavors.

Important research gaps found in the literature review are highlighted in Table 5. The detailed literature review evaluation from various research articles is covered in Section 4.

A CNN-based deep learning model called DEMNET was proposed by Murugan et al. [12] for the early examination of AD. Nevertheless, their study's limitations limit the possibilities for further investigation. In order to create a stand-alone framework for dementia screening and Alzheimer's diagnosis, Murugan et al. intend to advance their work by training and testing DEMNET on a variety of datasets. The Inception and Residual Networks are going to serve as the classifier's foundational models. Notably, omitting preprocessing stages like intensity

Table 4
The dynamics of article distribution according to its publisher.

Publisher	#Articles	#Conferences*	References
IEEE	16	3	9, 12, 24, 52, 55, 56, 61, 62, 66 & 54, 77, 80, 81, 87, 94, 98, 99 *
Elsevier	29	–	1, 2, 3, 6, 7, 8, 10, 11, 14, 16, 17, 19, 20, 23, 25, 28, 29, 30, 32, 38,39, 40, 41, 46, 48, 50, 86, 88, 92
Springer	19	–	4, 6, 13, 15, 18, 21, 22, 27, 36, 43, 44, 45, 53 [58], 82, 84, 90, 95, 101
Google Scholar	15	–	26, 31, 42, 57, 63, 69, 70, 72, 73, 74, 76, 78, 79, 91, 93
MDPI	17	–	33, 34, 35, 37, 49, 51, 59, 60, 64, 65, 68, 75, 83, 85, 89, 96, 100
Hindawi	2	–	47, 97

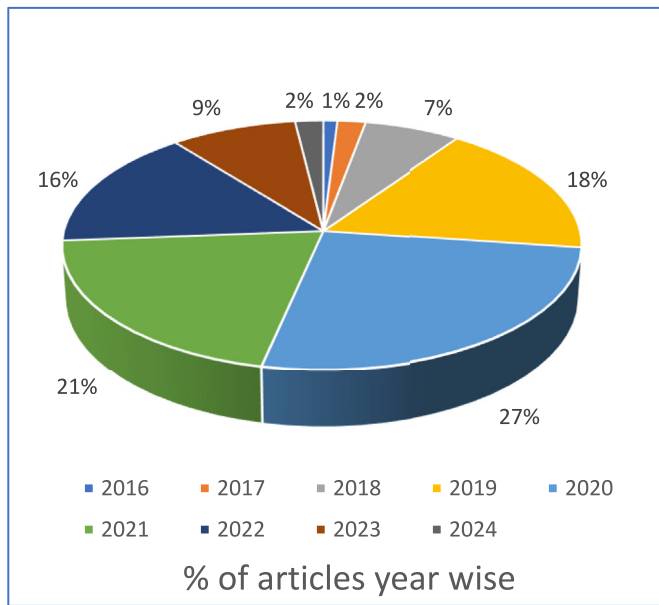


Fig. 2. Shows percentage of articles year wise.

normalization and skull stripping may yield results that are comparable to or even superior. If the dataset is big enough and the computer power is strong enough to handle the extra complexity, fine-tuning the pre-trained convolutional layers could help the model perform even better.

Zhang et al. [16] introduced a 3-D convolutional neural network for the classification of Alzheimer's disease, enhancing the convolution process to three dimensions to extract spatial information from MRI data. Various attention methods integrated features derived from each 3-D convolution layer with those from prior layers, ultimately aiding in the classification. Nonetheless, the approach exhibited numerous shortcomings. Despite decreasing the input data quantity by using MRI patches rather than complete brain pictures, model training continued to be computationally intensive. Furthermore, despite changing the model's parameters, such as the number of layers, dimensions, and count of kernels, achieving network convergence remained difficult. Decreasing the patch size to one-third of the original mitigated the non-convergence

problem and reduced the training duration. A balance between network parameters and configurations is essential to enhance classification efficiency and performance.

Mehmood et al. [26] introduced a transfer learning methodology for the early detection of AD utilizing MRI images. They applied layer-wise transfer learning to the VGG architectural family with weights that had already been trained. They could further refine their technique by integrating region-of-interest (ROI) modelling to enhance the efficacy of Alzheimer's disease detection. Sathiyamoorthi et al. [28] devised a computer-aided diagnosis system utilizing a deep convolutional neural network to predict Alzheimer's disease in MRI images. Although their technology demonstrates potential for diagnosing AD, the convolutional neural network layers require enhancement to improve performance. Zhang et al. [29] proposed a system for multiclass AD diagnosis with multimodal neuroimaging feature selection and integration. Nonetheless, their investigation encountered constraints, particularly regarding the storage of the kernel matrix when the subject count is extensive, necessitating considerable space. This issue happens a lot with other kernel-based methods, but the stochastic variance reduced gradient (SVRG) has been shown to work well at improving multiple kernel learning (MKL).

Shuangshuang and Lima [31] developed CNNs for image segmentation across datasets like ADNI, OASIS, and AIBL, this study aims to enhance AD diagnosis using deep learning methods, with a focus on refining diagnostic accuracy through deep learning, although improvement areas remain. Chen and Xia [32] employed iterative sparse and deep learning (ISDL) on ADNI data, this research delves into sparsity in multi-modal imaging data. Future studies are anticipated to explore sparsity-focused advancements for multimodal data enhancement. Tiwari et al. [33] developed an approach highlights the need for large datasets when using deep learning for disease detection. The study points out that deep learning methods generally require more data than hand-crafted feature extraction techniques. Alwakeel et al. [34] deep learning models have advanced AD diagnosis, this study using unspecified algorithms on AD datasets points to unresolved issues that need attention for further improvements in diagnostic techniques. Lin et al. [35] study uses CNN algorithms on genetic datasets (SNPs, DNA methylation, and gene expression) and identifies the absence of large, standardized benchmark datasets as a critical limitation, which restricts large-scale analysis. Arafa et al. [36] build a CNN-based machine learning approach on ADNI, this study primarily examines popular neuroimaging preprocessing methods but notes insufficient detail on machine learning methods, indicating an

Table 5

A synopsis of the most significant conclusions from the literature review.

Reference	Approach	Technique	Algorithm	Dataset	Limitations
[12]	Deep Learning	Convolution neural network	Optimization Algorithm	ADNI, MID, MOD, ND, VMD	If the data is sufficient and the resources can manage the added computational complexity, fine-tuning the pre-trained convolutional layers will improve the base model's performance.
[16]	Deep learning	Convolution neural network	Proposed Algorithm	Single modality dataset of structural MRI	Deep learning can reveal minute yet complex MRI picture features, which may aid AD diagnosis and prediction.
[26]	Transfer Learning Approach	Deep Learning	Machine learning	diffusion tensor imaging (DTI) dataset.	Potential future uses for the suggested model include lung and breast cancer screening.
[31]	Deep Learning	Convolution neural network	Image segmentation algorithm.	ADNI, OASIS, AIBL and other datasets	Continue to explore AD diagnosis methods on the basis of deep learning to improve further.
[32]	Deep Learning	Deep learning technique	Iterative sparse and deep learning (ISDL)	ADNI	Upcoming study will explore the sparsity in multi-modality imaging data.
[33]	Deep learning Approach	Machine Learning Techniques	Not Specified	Larger dataset	For disease detection, deep learning methods necessitate a larger dataset than handcrafted feature extraction methods.
[34]	Deep Learning	Deep learning technique	DL Algorithm	AD dataset	Despite the significant progress DL has made in AD diagnosis, there are still certain obstacles that require attention.
[35]	Deep Learning	Convolution neural network	Deep learning algorithms	SNPs, DNA methylation, and Gene expression datasets.	Key limitations identified in prior research, particularly the absence of extensive, standardized benchmark databases suitable for large-scale analysis.
[36]	Deep Learning	Convolution neural network	ML Algorithm	ADNI dataset	Only covered the most popular preprocessing methods for neuroimaging; Not provided enough information about ML.
[37]	Machine Learning	Convolution neural network	KNN algorithm	EEG dataset	Plan to improve the classification method to the point where all HC subjects are removed.

area for improvement. Weitschek et al. [37], provided a machine learning study with CNNs and the K-Nearest Neighbor (KNN) algorithm on an EEG dataset aims to improve classification methods. The goal is to enhance classification to exclude all healthy controls (HC) from detected subjects.

To address the limitations identified in our review and build upon the findings from our literature analysis, we have developed targeted improvement strategies detailed in Section 4.12. These strategies focus on enhancing data quality and accessibility, refining model architectures, and adopting more comprehensive data-sharing practices to improve AD diagnosis accuracy. By implementing these tailored solutions, our proposed framework aims to mitigate the challenges in data volume, algorithm complexity, and computational demands found in current approaches. This roadmap in Section 4.12 provides specific steps for advancing existing methodologies, fostering deeper insights, and driving further innovation in AI-based AD detection.

4. Discussion

In this part, a literature evaluation is conducted on the many approaches that are currently in use for diagnosing AD. It sheds insight on the numerous study issues that were mentioned in Section 2 of the dissertation.

4.1. Machine learning techniques

Researchers widely use machine learning (ML) techniques for AD research. Tiwari et al. [33] explored various diagnostic methods, including machine learning, biomarkers, and multi-modality approaches, and have made progress in detecting Alzheimer's disease (AD) with high accuracy. Structural MRI is crucial, and deep learning is effective but requires larger datasets. Weitschek et al. [37] observed that electroencephalography (EEG) signal analysis is essential for early dementia detection. A novel method using FIR filters and power intensity achieves high accuracy in distinguishing AD, MCI, and HC subjects. The method may enable low-cost real-time diagnosis. Future work will focus on refining and expanding this approach for broader clinical applications. Zhao et al. [38] introduce a method using spectrogram

features from speech data to identify Alzheimer's disease, aiding early detection and understanding. Pushkar et al. [43] found that diagnosis of AD is crucial for early intervention. A machine learning model using image processing achieved 90.25 % accuracy.

Lahmri and Shmuel [46] emphasize the critical importance of AD detection. Their research examines various features for AD classification, including cortical thickness and cognitive tests, finding that Support Vector Machines (SVM) using specific features outperformed other classifiers. Similarly, Sultan et al. [47] highlighted Alzheimer's as a major global concern, affecting millions. Their work utilized machine learning to detect

dementia in the OASIS dataset, with SVM providing the best results for early diagnosis and treatment. Future work will focus on expanding datasets and models to improve

reliability and system performance. Vibha et al. [54] pointed out a deficiency in early AD detection and introduced a Soft Voting Classifier that achieved 86 % accuracy in early AD diagnosis. Lastly, Hung Chang et al. [59] looked into how machine learning can be used with new biomarkers, like amyloid, tau protein, and NMDAR-mediated biomarkers, to help doctors make better diagnoses of AD. Their findings suggest that DL holds significant promise for predicting AD.

Liu et al. [69] improved the diagnostic accuracy of AD by 14 % through the application of instance normalization and model broadening to enhance 3D CNNs. However, their study faced limitations in terms of data processing and the dataset itself. Arya et al. [82] looked into how to use deep learning and machine learning on PET/MRI scans to find Alzheimer's disease. They talked about how effective these methods are while also pointing out problems like the need for certain modalities and

dataset overlap. Future research should focus on ensemble learning, explainable AI, and incorporating other modalities to improve robustness and accuracy. Balne and Elumalai [86] investigated AI strategies for diagnosing Alzheimer's, emphasizing the superiority of deep learning and ensemble learning over traditional methods. Their future work will aim to enhance model interpretability and incorporate diverse data modalities. Uddin et al. [101] analysed various machine learning models for Alzheimer's diagnosis, finding that the Voting Classifier achieved a 96 % accuracy rate. Future research will aim to further improve detection through feature optimization.

4.2. Deep learning methods

In order to diagnose AD, deep learning methods, especially sophisticated neural networks, have become crucial. Fernandez-Blanco et al. [1] emphasized the importance of early detection, using sagittal MRI scans and deep learning techniques to achieve promising results, particularly in the early stages of AD. Xiao et al. [2] used deep learning to improve medical computer-aided diagnosis (CAD). They used unsupervised CNNs to look at MRI images and were able to tell the difference between Alzheimer's and mild cognitive impairment (MCI) 97.01 % of the time. Nguyen et al. [3] proposed a novel machine learning system combining MRI analysis with activity monitoring for AD diagnosis, resulting in improved accuracy. Zerin Zenia et al. [4] highlighted that MRI has revolutionized brain research, with deep learning methods especially CNNs excelling in detecting neurological disorders such as Alzheimer's, Parkinson's, and schizophrenia.

Prabha and Chitradevi [5] studied automated brain sub-region segmentation for AD diagnosis, where Grey Wolf Optimization (GWO) achieved 98 % accuracy, emphasizing the hippocampus's significance in the process. Valliani et al. [22] discussed the transformative potential of deep learning in medicine, particularly neurology, aiding in disease diagnosis, image analysis, and data mining. However, challenges such as data privacy and quality remain, and collaboration among experts is necessary to maximize deep learning's potential in healthcare. Yuxiu Sui et al. [27] looked into how deep learning, specifically CNNs, could be used to quickly find AD in brain imaging data. They found that this method was more accurate than current best practices. However, they still need to address challenges such as slice selection, transfer learning, and hyperparameter optimization.

Sathiyamoorthi et al. [28] found that the biomedical field increasingly uses computer-aided diagnosis (CAD) to enhance Alzheimer's disease (AD) diagnosis. Their novel CAD system integrates image restoration, enhancement, region segmentation, feature extraction, and deep learning (DL) classification, offering better accuracy and efficiency than existing methods. Hwan Jin and Choi [30] created a deep CNN-based image interpretation system that uses PET scans to predict cognitive decline in people with MCI. This system worked better than previous ones and shows promise as a biomarker for prediction.

Shuangshuang and Lima [31] noted the growing use of deep learning for AD detection due to its high accuracy, discussing biomarkers, imaging techniques, and DL's potential in AD diagnosis. Chen and Xia [32] created the ISDL model, which uses deep feature extraction and sparse regression to make MRI-based diagnoses of AD and MCI more accurate, better than previous methods.

Alwakeel et al. [34] emphasized that Alzheimer's disease remains a major healthcare concern without a cure. While deep learning shows enormous promise for AD diagnosis, challenges such as overfitting and data quality remain. Their review explores AD diagnosis using deep learning, focusing on biomarkers and datasets, particularly CNN models applied to MRI and the ADNI dataset. DL is playing an increasingly important role in AD diagnosis and forecasting, according to Lin et al. [35]. This is especially true in neuroimaging and genomics.

Their review summarizes recent research, outlining challenges and future directions. Deep learning models offer potential not only for AD detection but also for personalized medicine, significantly impacting

global health.

Puente-Castro et al. [39] emphasized the importance of early-stage Alzheimer's detection. Their study utilized sagittal MRI images and transfer learning, demonstrating promising results in identifying the disease at its early stages. Brahimighahnavieh [40] noted that Alzheimer's disease (AD) is a leading cause of death. While deep learning significantly aids in AD detection, challenges remain in areas such as biomarkers, feature extraction, preprocessing, and model development. Xiao et al. [41] discovered that they can use unsupervised deep learning with convolutional neural networks (CNNs) to predict Alzheimer's from MRI images, achieving high accuracy on a large dataset.

Swathi and Ketki [44] focused on a deep convolutional neural network (DCNN) for Alzheimer's classification using MRI, with their model achieving an accuracy of 98.57 % and highlighting the potential for further enhancements. Abdelhalim et al. [48] emphasized the importance of non-invasive AD diagnosis, employing deep learning with 2D MR brain images, achieving an impressive 99.68 % accuracy in AD detection and staging.

Raees and Thomas [67] demonstrated a deep learning system using MRI scans to detect Alzheimer's disease early, achieving an accuracy between 80 and 90 %. While it has clinical and technological limitations, the system still outperforms traditional methods. Altwijri et al. [68] proposed the use of deep learning for AD diagnosis using MRI scans, achieving an impressive 99.3 % accuracy. Despite limitations in processing techniques and dataset size, its performance surpasses conventional models.

Ji et al. [72] improved Alzheimer's diagnosis by using deep learning with MRI imaging, leveraging ensemble learning with ConvNets to achieve exceptional accuracy. Future research should focus on improving feature extraction and addressing model robustness limitations. Yoon et al. [77] proposed a U-Net-based DL architecture for automated and accurate A β plaque recognition in mice brains. Future studies will aim to improve image processing and analysis techniques.

Latif et al. [75] developed a low-complexity DL model for AD diagnosis using MRI, though limitations include a small dataset and reliance on a single modality. Shastri et al. [83] showcased how deep learning techniques effectively classify and predict data for AD diagnosis. However, challenges such as data scarcity, overfitting, and the need for greater consistency and generalizability remain. To improve AD detection, future research should explore more advanced DL methods, such as 3D CNNs and Generative Adversarial Networks (GANs).

4.3. Multi-model or multi-class classification techniques

In AD diagnosis, the literature emphasizes the use of multiple models and multi-class classification methods. Zhang et al. [8] noted that accurately diagnosing AD remains a challenge. They presented a deep learning model that combines neuroimaging and clinical data, leading to improved diagnostic accuracy and outperforming other methods. Shaker et al. [11] talked about how important it is to be able to predict AD and showed how a multimodal multitask deep learning model can make it much easier to see how AD is getting worse, with promising results.

Weiguang Ding et al. [20] talked about how important it is to find AD early on. They suggested a deep learning framework that uses FDG-PET metabolism imaging to accurately tell the difference between MCI patients who aren't showing any signs of AD and those who are. Jiang et al. [29] tackled AD diagnosis through a novel multiclass classification framework based on neuroimaging data. The model incorporates regularization terms, feature selection, and kernel fusion to improve performance, though optimizing large datasets remains a challenge.

Venugopalan et al. [42] discovered that using deep learning to combine MRI, genetic, and clinical data makes it easier to classify the different stages of Alzheimer's disease. This model does a better job than others and gives us new information about how the disease gets worse.

Alves et al. [74] demonstrated that applying deep learning to brain connection matrices derived from EEG data outperforms traditional

methods in diagnosing schizophrenia and Alzheimer's disease, despite some limitations related to the dataset. Ullah and Jamjoom [76] introduced a convolutional neural network (CNN) model that achieves an impressive 99.38 % accuracy in diagnosing different stages of Alzheimer's disease using MRI data. They emphasized the need for future studies to explore transfer learning strategies and utilize larger datasets for further improvement.

Yang et al. [95] noted the potential of deep learning-based speech analysis for Alzheimer's screening, although it remains challenging to interpret and requires more data. The accuracy of these models is only 85 % of conventional methods. Hussain et al. [94] presented a 12-layer CNN model that attained a 97.75 % accuracy rate for Alzheimer's detection, outperforming previous models. Future research in this area will primarily focus on early detection and multi-class classification to enhance diagnostic capabilities.

4.4. Hybrid learning and feature engineering

In the literature, feature engineering and hybrid approaches were found to be useful for AD diagnosis. Nawaz et al. [15] focused on AD diagnosis and staging using deep transfer learning. Pre-trained Alex Net extracts deep features for multiclass classification, outperforming other methods with 99.21 % accuracy. Jiang et al. [29] address Alzheimer's disease diagnosis with a novel multiclass classification framework using neuroimaging data. It introduces regularization terms, feature selection, and kernel fusion, demonstrating improved performance. Challenges include efficient optimization with large datasets.

Anandhavalli et al. [51] focused on early AD detection using a hybrid DL approach. The system achieves a remarkable 98.5 % accuracy in distinctive cognitively usual controls from early MCI. Deep neural networks show potential in discovering AD biomarkers from imaging data. The study proposes a multimodal DL approach for AD detection. AL-SHOUKRY et al. [52] found that the treatment is accurate for diagnosing AD in crucial situations. DL aids early AD diagnosis by analyzing MRI data and using machine learning (ML) and DL techniques with various datasets. The study explores AD history, ML to DL transition, AD modules, datasets, and highlights research focusing on biomarkers, neuroimaging, and image analysis.

Buwaneswari and Gayathri [53] suggested a deep learning approach using SegNet for brain feature segmentation and ResNet-101 for AD classification. It achieves 96 % sensitivity and 95 % accuracy in AD detection, surpassing traditional SVM methods. The segmentation process improves classifier performance, enhancing AD diagnosis. Rabia Shakir et al. [60] used ontologies to improve Alzheimer's disease understanding and early detection using deep learning, achieving an accuracy of 94.61 %.

Liang and Gu [96] The ADGNET framework achieves great performance and may help with future medical diagnosis by using poorly supervised learning for Alzheimer's identification with minimum annotations. Faisal and Kwon [98] created a CNN-based technique that uses sMRI to diagnose Alzheimer's disease early and achieves better accuracy while requiring less complexity. Future work will incorporate pre-processed photos and patient history. Fritsch et al. [99] improved early Alzheimer's screening with an accuracy rate of 85.6 % by applying neural network language models to evaluate speech patterns. Future studies will address errors related to speech recognition and language assistance. Mohammed et al. [100] used the OASIS and MRI datasets to test machine learning techniques for diagnosing dementia. They found that hybrid models (AlexNet + SVM) work better, with a 94.8 % success rate. Future studies should validate the findings and look at more model enhancements.

Xue C et al. [103] focused on developing an AI-based framework for differential diagnosis of dementia. The presented model integrates a wide array of data sources, including demographic information, personal and family medical histories, neuropsychological assessments, medication use, and multimodal neuroimaging. It aims to improve the accuracy of

dementia diagnosis by identifying the underlying causes across various etiologies, such as AD, vascular dementia, and others, it performed remarkably well, achieving a high micro-averaged AUROC of 0.94 for diagnosing dementia and 0.96 for distinguishing between different types. This AI model's diagnostic power was even shown to outperform human neurologists in certain cases when augmented with AI support. Its ability to handle mixed cases of dementia, which involve co-occurring pathologies, adds a valuable tool for clinicians in complex diagnostic scenarios., this model offers the potential to be used as a screening tool in clinical environments and drug trials, supporting more personalized and effective dementia management strategies.

4.5. Deep learning using fMRI imagery

Different imaging techniques are possible in healthcare. fMRI is one such imaging technology. Using spatial and temporal information from fMRI information, Chen et al. [7] developed a 4-D DL model (C3d-LSTM) for Alzheimer's diagnosis.

Thanh Duc et al. [13] studied how to employ 3-D deep learning on RS-fMRI data to diagnose Alzheimer's disease and predict MMSE scores accurately. Nagaraj et al. [49] observed that DL aids in AD diagnosis through brain MRI segmentation and classification. It offers improved accuracy and efficiency.

Salomón et al. [50] employed mobility data and DL models to identify AD stages, facilitating monitoring and treatment planning. Guo and Zhang [55] used advanced computerized healthcare that leverages diagnostic imaging and deep learning. For early AD detection, a specialized deep learning algorithm (IDLA) uses clinical and MRI data. This approach aims to enhance diagnostic accuracy by approximately 25 %.

Hussain et al. [56] opined that AD is an incurable brain ailment affecting reminiscence and cognitive abilities. Deep learning-based CNN models improve detection.

Yue et al. [71] demonstrated that AD and MCI may be successfully and precisely identified using deep convolutional neural networks (DCNNs). Future studies will focus on anticipating the path of disease. Among the restrictions are differences in classification accuracy and reliance on baseline MRI images. Altinkaya et al. [73] illustrated how deep learning and super-resolution may enhance the quality of MRI images, helping to diagnose dementia and Alzheimer's disease. Future work should focus on improving AI techniques and addressing image processing difficulties.

Zhu et al. [81] detect important brain characteristics from sMRI images; the DA-MIDL model improves early Alzheimer's diagnosis. The model has fixed patch sizes and lacks end-to-end integration. These issues will be the focus of future research projects. Ahila et al. [84] disclosed the 96 % successful CAD method for CNN-based early Alzheimer's disease (AD) identification. Future research will employ neural networks, utilizing multiple data sources.

Fong et al. [87] offered deep learning object detection methods with outstanding accuracy for diagnosing Alzheimer's disease without MRI pre-processing. Future studies, examining hippocampal segmentation, will include data on moderate cognitive impairment.

Basaia et al. [88] proved that CNNs can accurately diagnose Alzheimer's and moderate cognitive impairment without the need to first remove data from MRI images. Future research should focus mostly on preclinical identification and atypical AD signs.

Saratxaga et al. [89] offered a deep learning method with excellent accuracy for diagnosing Alzheimer's using MRI data. Subsequent studies will use larger datasets and examine additional stages of the disease. Noor et al. [90] showed how effective deep learning, and CNNs in particular, was for diagnosing neurological illnesses based on MRIs. Challenges include dataset limits, real-time prediction, and adversarial noise. Future research should address these issues.

Salehi et al. [91] Deep learning techniques, and CNNs in particular, outperform MRI-based Alzheimer's diagnosis. To enhance early

detection, more research should use sophisticated methods and a variety of datasets.

4.6. Techniques used for early diagnosis

Early diagnosis of AD enables better care and treatment planning. Pan Zhou et al. [9] introduce the advances in deep learning that enable early Alzheimer's diagnosis by combining brain network data and clinical information with high accuracy and stability. Murugan et al. [12] opined that progress in AD detection is crucial. A Convolutional Neural Network (CNN) model detects AD stages accurately.

A study by Rathore and Janghel [14] used pre-processing and VGG-16-based CNN on ADNI fMRI and PET datasets to increase the accuracy of diagnosing AD. The model achieves high accuracy, especially with SVM and K nearest classifiers. Yong Fan et al. [17] proposed a DL model based on MRI scans that predicts progression from MCI to AD with high accuracy, aiding early prognosis.

Weiguang Ding et al. [20] stated that early diagnosis of AD is vital. With high accuracy, a DL framework using FDG-PET metabolism imaging distinguishes pre-symptomatic AD from non-AD MCI subjects. Haibo and Xiaojun [23] opined the diagnosis of AD is vital. It also introduces a multi-task learning approach using EEG images, bridging feature extraction and classification. It shows promising results in early AD detection. Mehmood et al. [26] observed that deep learning aids in early Alzheimer's detection through layer-wise transfer learning and brain image segmentation. Impressive classification results were obtained.

According to Arafa et al. [36], AD is a foremost health apprehension with limited diagnostic tools. It explores recent deep learning-based approaches for early AD detection, emphasizing imaging, pre-processing, and classification challenges. Key contributions include introducing the diagnosis process, discussing brain imaging modalities, highlighting research challenges, and offering directions for future studies. The survey addresses the critical need for accurate AD detection and classification.

Weitschek et al. [37] observed that electroencephalography (EEG) signal analysis is essential for early dementia detection. A novel method using FIR filters and power intensity achieves high accuracy in distinguishing AD, MCI, and HC subjects. The method may enable low-cost real-time diagnosis. Future work is to refine and expand this approach for broader clinical applications.

Venugopalan et al. [42] found that deep learning integrates MRI, genetic, and clinical data to classify Alzheimer's disease stages, outperforming other models and offering new insights. Pushkar et al. [43] stated that the diagnosis of AD is crucial for initial intervention. A machine learning model using image processing achieved 90.25 % accuracy. Amira et al. [45] observed that detection of Alzheimer's disease (AD) is crucial. A deep learning framework using CNNs classifies AD stages with high accuracy and offers a remote diagnosis web application.

Vibha et al. [54] found that detection of this AD lacks in the early stages. The study introduces Soft Voting Classifier, achieving an 86 % accuracy rate for early AD detection. Rusinek et al. [57] opined that early AD detection is vital. A 3D deep learning model using structural MRIs distinguishes mild AD, MCI, and normal individuals with an 85.12 AUC. Gamal et al. [80] suggested employing an ensemble learning approach, and the outcomes provide good AUC values for early diagnosis of AD based on MRI data. The next study intends to include clinical data to increase accuracy.

Zhang et al. [102] explores the joint effect of various modifiable risk factors on dementia risk by analysing data from 344,324 participants in the UK Biobank. The researchers identified 210 modifiable factors linked to dementia and assessed their combined influence using a multivariate Cox model, categorized these factors into domains like lifestyle, medical history, and socioeconomic status, finding that these three domains contribute significantly to dementia risk. The study estimated that by addressing these risk factors, up to 47–72 % of dementia cases could potentially be prevented. This highlights the importance of public health interventions focused on lifestyle improvements and early medical

intervention.

Lee et al. [104], which focuses on creating an AI-based predictive model for the early detection of AD. The model, developed using cognitive tests and MRI scans, leverages the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset. The study highlights the model's accuracy (81.66 %) and generalizability across real-world clinical environments in the UK and Singapore. One of its significant strengths is its transparency, allowing clinicians to understand the underlying mechanisms of the AI's predictions, which is crucial for adoption in clinical settings.

The PPM outperforms traditional clinical assessments in early dementia prediction and improves the accuracy of detecting Mild Cognitive Impairment (MCI) to AD progression. It also suggests expanding the model to predict various dementia subtypes and including more diverse datasets to enhance its global applicability. The model's integration of the Generalized Metric Learning Vector Quantization (GMLVQ) framework strengthens its prediction capability and adaptability across different clinical settings.

4.7. Ensemble or transfer learning methods

Ensemble and transfer learning approaches are found to enhance efficiency in AD detection. Diacono et al. [10] stated that early Alzheimer's detection using structural MRI for mild cognitive impairment (MCI) is essential. Deep learning strategies prove effective. Thanh Duc et al. [13] study and employ 3-D deep learning on RS-fMRI data to diagnose Alzheimer's disease and predict MMSE scores accurately. Liang et al. [16] used a novel deep learning approach using densely linked CNN with connection-wise attention for efficient AD detection and prediction, achieving high classification accuracy of 97.35 % for AD vs. NC, 87.82 % for cMCI vs. NC, and 78.79 % for cMCI vs. ncMCI.

Zhang et al. [18] observed that diagnosis of Alzheimer's disease (AD) is vital. Deep 2D convolutional neural networks on MRI images are producing promising results for AD classification. Yang et al. [19] focused on ensemble deep learning, which integrates multiple deep learning algorithms for Alzheimer's disease classification, outperforming other ensemble approaches. It draws on multisource data and experts' wisdom.

Islam and Zhang [21] observed that the diagnosis of Alzheimer's disease (AD) is challenging. A deep learning model for AD diagnosis using MRI data shows promise, particularly for early-stage diagnosis. MEFRAN KHAN [24] focused on detecting Alzheimer's disease using MRI data. Transfer learning, using a pre-trained VGG architecture, proves effective in reducing the reliance on large training sets, yielding state-of-the-art results. The study also explores layer-wise fine-tuning and data selection based on image entropy. The proposed approach shows promise for Alzheimer's diagnosis, as well as potential applications in other medical diagnosis fields.

Mehmood et al. [26] discovered that deep learning aids in early AD detection through layer-wise transfer learning and brain image segmentation. Impressive classification results were obtained.

Mujahid et al. [85] proposed an ensemble deep learning model with 97.35 % accuracy for Alzheimer's detection using balanced MRI datasets. Future work will primarily focus on incorporating a variety of data types for improved diagnosis.

Suganthi et al. [78] built VCNN and DCNN models and attained over 90 % accuracy in classifying Alzheimer's stages based on MRI scans. Subsequent investigations will examine other perspectives from MRI and improve the model parameters. Roy et al. [79] suggested a CNN model that can identify Alzheimer's disease MRI images with 80 % accuracy. Later research will focus on improving computation and increasing accuracy with more data.

Li et al. [92] used MOST images and CNNs in a deep learning strategy to count neurons in the brains of AD mice, yielding respectable results. However, the challenge of handling noise and large data sets remains. Future research will concentrate on unsupervised learning and noise

reduction techniques. Mehmood et al. [93] proposed two CNN-based models for early AD diagnosis using segmented MRI data. The models' accuracy rate is great, but they struggle with data management and generalization.

4.8. Alzheimer's detection using 3D data

This section focuses on the AD detection methods based on 3D data.

Aruchamy et al. [61] focused on a novel 3D MR image technique that identifies Alzheimer's disease via statistical features and achieves 90.9 % accuracy with classifiers. Yang et al. [62] suggested a new unified CNN framework that combines 3D CNN and 3D CLSTM to find Alzheimer's. On the ADNI dataset, this framework worked 94.19 % of the time. Selvaraj et al. [63] observed that deep learning aids Alzheimer's detection. The proposed AD-3DCNN model achieves 97.53 % accuracy, surpassing existing pre-trained models.

Fig. 3 provides an overview of the AD detection process using 3D data.

Agarwal et al. [64] found that end-to-end learning with CNN models achieves high accuracy in classifying AD vs. CN and SMCI vs. AD phases. Ali et al. [65] use DL and multimodal MRI together to get a better picture of AD. They get 98.21 % accuracy by using 3D-CNN to represent biomarkers. Ehsan et al. [66] showed that precise AD diagnosis depends on brain feature classification. In terms of predicting AD, the 3D CNN outperforms traditional classifiers.

Feng et al. [70] showed that when utilizing MRI to AD diagnose and MCI, 3D-CNN-SVM performs better than other models in terms of high accuracy. There are two disadvantages: the lack of follow-up information and the use of baseline MRI. Huang et al. [97] proposed a 3-D CNN + SVM model for early Alzheimer's diagnosis using PET imaging, which demonstrates good performance but faces constraints due to a lack of training data. Future work will enhance MCI categorization.

4.9. Role of LLMs in AD detection

One area where Large Language Models (LLMs) show promise is in the diagnosis of AD. Cognitive decline can be more easily detected in its early stages with the help of LLMs, which analyze unstructured data such as patient speech and physician notes. Their capacity to integrate multimodal data improves predictive modeling for illness progression, and their natural language processing (NLP) skills aid in the identification of linguistic markers. By automating data interpretation and streamlining Clinical Decision Support Systems (CDSS), LLMs further enhance diagnostic accuracy. Researchers benefit from LLMs because they help to summarize large amounts of AD-related literature, find gaps, and propose new research areas, all of which contribute to the advancement of AD detection and treatment.

4.10. Datasets used in AD detection Research

The review of the literature highlights the extensive use of specific datasets in AD detection research, showing the significance of data diversity in advancing diagnostic methods. The **ADNI (Alzheimer's Disease Neuroimaging Initiative)** dataset, one of the largest and most frequently referenced datasets, is frequently used in combination with other datasets due to its comprehensive collection of neuroimaging, genetic, and clinical data. It allows for a broad exploration of AD at different stages, including mild cognitive impairment (MCI) and dementia. ADNI is referenced in many studies, as seen in the majority of the citations in the table.

The **OASIS (Open Access Series of Imaging Studies)** dataset is another widely used resource, particularly valued for its freely available neuroimaging data. Many studies have utilized OASIS alongside ADNI to improve diagnostic algorithms and validate findings across datasets, ensuring robustness.

Some studies also explore less traditional datasets like smartphone-

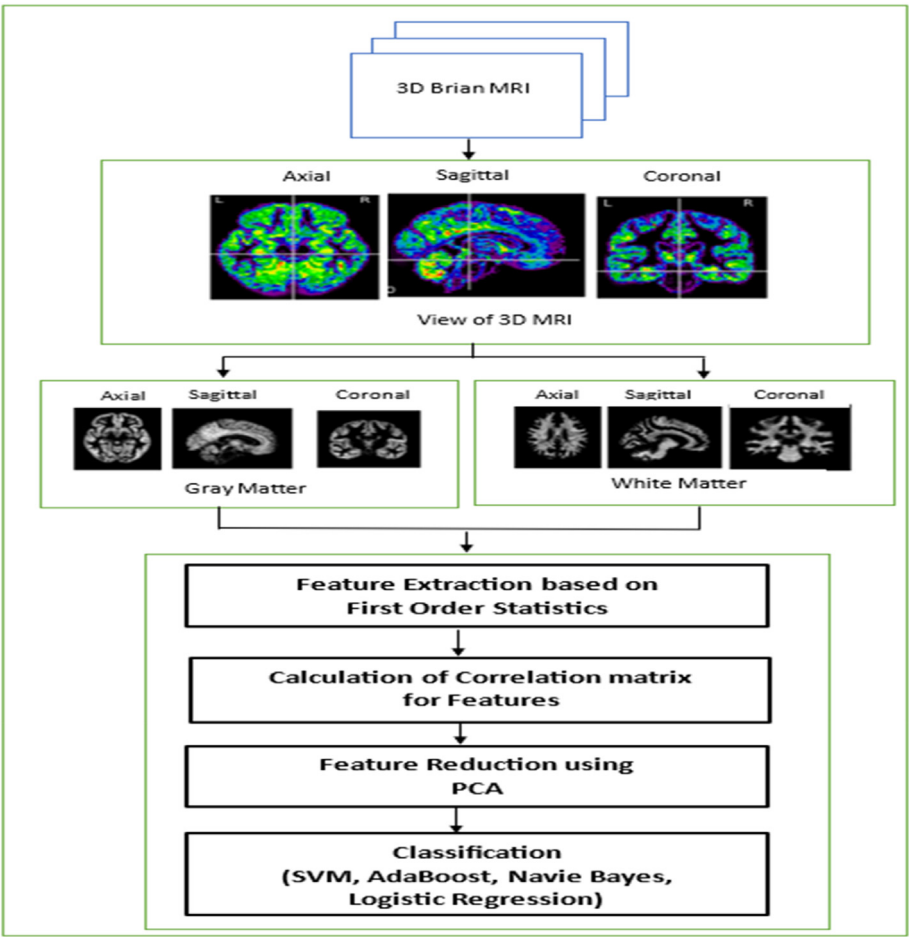


Fig. 3. Overview of AD detection using 3D data [61].

based sensors for early AD detection through behavioral data, which provides insights into potential non-invasive diagnostic methods.

The **ImageNet** dataset, though not directly linked to medical imaging, has been used for transfer learning methods where models pre-trained on large, generic datasets are adapted to medical applications.

Other combinations like MRI and ADNI also reflect the importance of multimodal approaches, where neuroimaging data from different modalities help improve diagnosis accuracy. Table 6 presents ANDI as the most widely used dataset in the literature. OASIS is another dataset used in many research papers.

4.11. Performance metrics

ML and DL models find widespread use in AD research. The performance evaluation is based on standard metrics such as precision, recall, F1-Score, and accuracy, as used in a number of articles such as [1,5,8],

Table 6
Datasets used for AD detection in the literature.

Reference	Dataset
[1,4,31,34,39]	ADNI and OASIS data sets
[2,6,7,12–14,17,20,22,24,26,29,30,32,35,36,38]	ADNI
[41–46,48,62–65]	
[3]	Smartphone Based Single and multi-sensor-based dataset
[15,18,21,27,47]	OASIS
[5,49,66]	MRI and ADNI
[25]	ImageNet dataset

and [6], to name a few. These metrics are based on the confusion matrix presented in Fig. 4.

True positive (TP), false positive (FP), false negative (FN), and true negative (TN) are some of the measures that are used to describe the confusion matrix and its ground truth and predicted labels. These are shown in Equations (1)–(4).

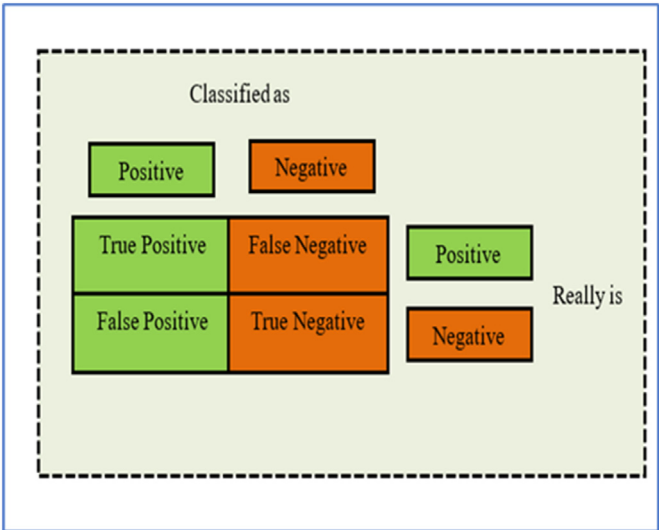


Fig. 4. Confusion matrix.

$$\text{Precision (p)} = \frac{TP}{TP + FP} \quad (1)$$

$$\text{Recall (r)} = \frac{TP}{TP + FN} \quad (2)$$

$$F1 - \text{score} = 2 * \frac{(p * r)}{(p + r)} \quad (3)$$

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN} \quad (4)$$

$$AUC = \frac{1}{2} \left(\frac{TP}{TP + FN} + \frac{TN}{TN + FP} \right) \quad (5)$$

The subsequent measurement is referred to as the area under the curve (AUC). With the goal to gain an understanding of the performance of learning-based models, we make use of Equation (5). The effectiveness of the models that are utilized in the AD detection process can be better understood with the assistance of these performance measures.

4.12. Recommendations

To enhance the diagnosis of AD, it is essential to optimize current models, broaden datasets, and implement research findings in practical contexts. Here is a summary of essential techniques to enhance existing methodologies:

Model Optimization.

- **Enhancing Algorithm Performance:** Implement the new architectures like transformers or hybrid models by combining the CNNs presented in section 4.3 and section 4.4 and fine-tuning hyperparameters presented in section 4.7 by ensemble the models to capture the complex patterns in imaging data, so that this can improve the accuracy and trustworthiness of machine learning and deep learning models.
- **Reducing Computational Complexity:** Simplify models using the techniques like pruning, quantization, or knowledge distillation used in Zhu et al. [81] can reduce computational requirements, making models more practical for everyday clinical settings, so they are easy to use in clinical settings without lowering their quality
- **Automated Machine learning for continuous hyper parameter tuning and optimization,** which can adapt to varying dataset sizes and complexities covered in sections 4.2, 4.5 and 4.7. AutoML techniques such as Bayesian optimization could significantly reduce tuning time while enhancing model performance in real-time applications are covered in Refs. [10,25,35].

Expanding Datasets.

- **Data Augmentation:** Use methods for augmentation to make datasets bigger and model generalization better, by going beyond traditional transformations (e.g., flipping, rotation) to include generative adversarial networks (GANs) or synthetic data generation are covered in section 4.2. GANs can create diverse and realistic images, effectively increasing the training set's robustness without requiring additional costly data collection.
- **Collaborative Data Sharing:** Encourage partnerships to create larger, more diverse datasets like federated learning approaches, this approach allows for training on a vast array of diverse datasets without transferring sensitive patient data, thereby maintaining privacy while ensuring generalizability across populations.
- **Incorporating Multimodal Data:** Combine data from different modalities (e.g., imaging, genetics) to enhance diagnostic accuracy covered in section 4.3, 4.8 and 4.10.

Real time Applications of Research Findings.

- **Clinical Decision Support Systems (CDSS):** Integrate AI models into CDSS for early detection, supporting healthcare professionals in diagnosis.
- **Personalized Medicine:** Tailor treatment plans using AI models for more effective therapies.
- **Public Health Strategies:** Leverage AI to guide public health initiatives like screening and resource allocation for better AD management.

5. Conclusion

This paper offers a comprehensive systematic review of 104 peer-reviewed articles published between 2016 and 2024, focusing on advancements in Alzheimer's disease (AD) diagnosis through artificial intelligence (AI). The review synthesizes key findings from studies that employ machine learning, deep learning, ensemble models, and transfer learning for early AD detection.

By addressing multiple research questions, this review highlights the current state of AI-enabled diagnostic methods while identifying significant research gaps. The paper provides valuable insights into how different approaches have contributed to improving AD diagnosis. It also identifies areas where further exploration is needed to enhance these techniques, paving the way for the development of more efficient, computer-based detection methods.

Overall, this work serves as a foundation for future research, aimed at refining AI methodologies and improving AD diagnosis accuracy.

CRediT authorship contribution statement

Radhakrishna Chamakuri: Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Hyma Janapana:** Validation, Supervision.

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