Exploring Angiogenesis and Artificial Intelligence in Alzheimer's Disease: Implications for Early Detection and Therapeutic Strategies

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Abstract

Background: Alzheimer's disease (AD) presents a significant global health challenge, affecting millions and imposing substantial socioeconomic burdens, with healthcare costs exceeding US$100 billion annually. The disease's complexity is underscored by its slow progression and the pivotal role of amyloid plaques in its pathology. Despite advancements in understanding AD, critical questions regarding the mechanisms of amyloid plaque development and their relationship with neuroinflammation and angiogenesis remain. Methods: This study employed advanced imaging techniques and artificial intelligence (AI) to investigate the interplay between amyloid beta (Aβ) accumulation, neuroinflammation, and angiogenesis in AD. Magnetic resonance imaging (MRI) facilitated detailed assessments of brain structure alterations, while machine learning models enhanced diagnostic accuracy by analyzing imaging data and identifying patterns linked to disease progression. Results: The findings revealed a significant association between Aβ deposition and increased angiogenesis, contributing to neurovascular dysfunction and exacerbating neuroinflammation. AI-driven analyses demonstrated improved diagnostic capabilities, detecting early changes in brain structure associated with mild cognitive impairment (MCI) and AD. Specifically, convolutional neural networks (CNNs) such as AlzheimerNet achieved remarkable accuracy in distinguishing AD from other neurodegenerative conditions. Conclusion: This research underscores the multifaceted nature of AD, highlighting the critical roles of amyloid plaques, neuroinflammation, and angiogenesis. The integration of AI and advanced imaging modalities offers promising avenues for early diagnosis and intervention, potentially transforming patient management strategies. Continued exploration of these pathways may yield effective therapeutic targets to mitigate the progression of AD and enhance patient outcomes.

Keywords: Alzheimer's Disease, Angiogenesis, Artificial Intelligence, Early Detection, Neuroinflammation.

Significance | This review discusses the understanding the interplay of angiogenesis and Aβ in Alzheimer's could lead to innovative AI-driven diagnostics, enhancing early intervention strategies.

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Introduction

Alzheimer's disease (AD) has emerged as one of the most pressing health challenges of our time, affecting millions globally. The neurodegenerative disorder is particularly alarming due to its slow progression, complex pathology, and immense socioeconomic burden. Approximately 10% of the global population suffers from AD, and healthcare costs associated with managing the disease

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exceed US$100 billion annually, creating significant strain on medical systems worldwide (Ahmad et al., 2020). The disease's toll extends beyond economic impact, inflicting immense human suffering on individuals and their families. Despite significant strides in understanding AD, key questions remain unanswered, particularly concerning the development of amyloid plaques, a hallmark of the disease (Wu et al., 2023). These plaques, composed primarily of c-amyloid peptide fragments, are central to AD pathology and have been linked to molecular lesions, brain inflammation, genetic factors, cerebral hypoperfusion, and hereditary influences (Fang et al., 2023).

One of the striking features of AD is the increased angiogenesis observed in the brain, a process that is closely tied to neurodegeneration and neuroinflammation. The Aβ peptide, a primary constituent of amyloid plaques, negatively affects both neurons and vascular cells, including endothelial and smooth muscle cells (Lehrer & Rheinstein, 2022). Aβ deposition in the brain may contribute to hypoxia, leading to vascular dysfunction, which, in turn, induces inflammation and stimulates angiogenesis (Yu et al., 2020). The pathological angiogenesis that arises from these processes exacerbates neuroinflammation by allowing blood components to leak into the brain, potentially worsening AD symptoms (Fasoli et al., 2021). This feedback loop between vascular dysfunction, angiogenesis, and neuroinflammation highlights the complex interplay of factors driving AD progression.

Interestingly, emerging evidence suggests that Aβ may directly trigger inflammatory responses, independent of vascular dysfunction (Ahmad et al., 2020). Given the close relationship between inflammation and angiogenesis, it is plausible that Aβ could directly induce angiogenesis before any observable vascular impairments. This notion has led to the hypothesis that angiogenesis, spurred by excessive Aβ accumulation, may be a precursor to AD pathogenesis. If true, this pathway presents new opportunities for therapeutic interventions aimed at halting or reversing disease progression in its early stages (Lehrer & Rheinstein, 2022).

Neurovascular dysfunction has long been recognized as a key contributor to AD, and several studies have explored the mechanisms by which abnormal blood vessel growth may contribute to neurodegeneration (Ahmad et al., 2020). Vascular endothelial cells in the brain secrete neurotoxic proteins that, along with beta-amyloid plaque precursors, lead to neuron death in the cortex, further contributing to cognitive decline in AD patients (Bowirrat, 2022). The activation of endothelial cells through angiogenesis, triggered by inflammation and hypoxia, suggests that targeting these cells could be a promising approach in AD treatment. Developing anti-angiogenic drugs that specifically target the abnormal endothelial cells in the AD brain may hold the key to addressing the vascular component of the disease (Ahmad et al., 2020).

Over the last few decades, artificial intelligence (AI) has emerged as a powerful tool in the field of neurology, particularly in the study, diagnosis, and treatment of neurodegenerative diseases such as AD. With dementia accounting for 60% to 70% of AD cases, the potential for AI to revolutionize early detection and diagnosis is immense (Abduljawad et al., 2022). The chronic nature of AD, characterized by its gradual worsening of cognitive and behavioral functions, makes early diagnosis crucial for slowing disease progression and minimizing its impact on individuals and society (George et al., 2022). Computer-aided diagnostic (CAD) systems, powered by AI, have the potential to detect subclinical changes, provide insights into underlying mechanisms, and guide the development of neuroprotective therapies that may prevent or delay disease progression (Bhatele et al., 2022). These systems, which incorporate neuropsychological evaluations and advanced imaging techniques, offer new ways of monitoring and interpreting brain activity in AD patients (Khaliq et al., 2023).

Magnetic resonance imaging (MRI) has been one of the most valuable tools in the diagnosis and study of AD. MRI provides high-resolution, detailed images of brain structures, allowing clinicians and researchers to observe changes in the brain associated with AD. Structural MRI, in particular, has proven effective in detecting alterations in brain structure in individuals with mild cognitive impairment (MCI), a condition often considered a precursor to AD (Litvinenko & Lobzin, 2022). Research has shown that patients with MCI who later develop AD exhibit significant atrophy in key brain regions, such as the medial temporal lobes and posterior cingulate cortex, compared to healthy controls or patients with stable MCI (Maiese, 2023). These findings underscore the importance of early detection in AD, as structural changes in the brain can provide valuable clues about the disease's progression.

AI's integration into diagnostic processes has further enhanced the accuracy and speed of AD diagnoses. By analyzing vast amounts of data from MRI scans and other diagnostic tests, AI systems can identify subtle patterns that may not be immediately apparent to human observers (Ratan et al., 2023). This ability to process and interpret large datasets in real-time enables more efficient and precise monitoring of neurodegenerative diseases, ultimately improving patient outcomes (Jung & Damoiseaux, 2024). The potential for AI to contribute to the early detection of AD is particularly exciting, as early intervention is critical for slowing disease progression and improving the quality of life for patients.

AD is a multifaceted disease characterized by complex interactions between amyloid plaques, neuroinflammation, angiogenesis, and vascular dysfunction. While significant progress has been made in understanding these processes, key questions remain unanswered, particularly regarding the direct role of Aβ in angiogenesis and neuroinflammation. AI and advanced imaging techniques offer new avenues for early diagnosis and treatment, providing hope for

mitigating the devastating effects of AD. Future research will continue to explore these pathways, with the goal of developing more effective interventions to slow or halt the progression of this debilitating disease.

2. Literature Review

Recent studies have investigated advanced imaging techniques and machine learning (ML) models to enhance the diagnosis of neurodegenerative disorders, particularly Alzheimer's disease (AD) (Wang et al., 2022). Optical coherence tomography (OCT) has been used to examine retinal changes in AD patients, with findings indicating that macular thickness and volume correlate with AD severity and biomarkers. These results underscore the potential of OCT, when combined with ML models, as an effective diagnostic tool for AD. Moreover, the study identified the most efficient ML models for diagnosing AD based on retinal thickness (Wang et al., 2022).

Another study developed a deep learning-based model to distinguish between various tauopathies, including AD, progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), and Pick's disease (PiD) (Koga et al., 2022). The research employed a YOLOv3 object detection system to classify five distinct types of tau inclusions, with a random forest classifier correctly identifying 29 of 30 cases, achieving an average test score of 0.97. This highlights the efficacy of deep learning models in classifying different neurodegenerative diseases using digital histological images (Koga et al., 2022).

The application of machine learning in analyzing biomarkers and clinical symptoms related to neurodegenerative diseases has also been explored (Khaliq et al., 2023). Techniques such as neuroimaging and motion tracking, coupled with deep learning algorithms like neural networks, allow for monitoring brain structure changes, motor symptoms, and cognitive decline. This approach significantly enhances the diagnostic capabilities for diseases like AD and Parkinson's (Khaliq et al., 2023).

In addition, plasma biomarkers, such as β-amyloid, tau, and neurodegeneration markers, have been studied in the context of AD diagnosis (Sun et al., 2022). These biomarkers play a critical role in improving diagnostic models for moderate to severe AD dementia. While few studies have focused on plasma inflammatory markers, the research emphasizes the importance of blood-based biomarkers in AD diagnosis (Sun et al., 2022).

ML algorithms have also been used to classify neurodegenerative disorders using blood transcripts (Huseby et al., 2022). Small sets of transcripts were identified, demonstrating high sensitivity and specificity in distinguishing between diseases. The findings suggest the potential for a blood-based, non-invasive, and cost-effective screening method for neurodegenerative disorders (Huseby et al., 2022).

Finally, capsule networks have been shown to outperform deep transfer learning models in classifying AD, Parkinson's disease, and healthy controls. With impressive accuracy, capsule networks present a promising tool for early screening of neurodegenerative disorders (Bhatele et al., 2022).

3. Methodology of AI Model

Artificial Intelligence (AI) and Machine Learning (ML) have revolutionized various sectors, including healthcare, by enhancing the accuracy and efficiency of disease detection and medical service delivery. In the field of neurodegenerative disorders, particularly Alzheimer's disease (AD), AI and ML have been instrumental in automating diagnosis using advanced imaging techniques like structural magnetic resonance imaging (MRI). This discussion explores the role of AI and ML in detecting AD using structural MRI, emphasizing conventional ML methods and the process of feature extraction and classification for improved diagnostic accuracy.

The complexity and abundance of brain imaging data create a significant challenge for medical professionals. The intricacies of brain structures necessitate a thorough and accurate analysis, which can be tedious and error-prone when reliant solely on human expertise. Doctors, in their assessments, often apply subjective judgment, which might lead to inconsistencies and missed diagnoses. Therefore, the demand for quantitative, objective measurements in neuroimaging has become paramount, especially for diseases like AD. Recent advancements in image processing have introduced computer-aided diagnostic (CAD) systems, which complement traditional medical image analysis by offering precise, consistent, and timely diagnostic solutions. CAD systems are particularly valuable for reducing the burden on radiologists and enhancing diagnostic accuracy, making them a critical asset in the detection of AD.

The use of CAD in detecting Alzheimer's disease has gained attention, particularly in recognizing AD's progression from early stages. AD diagnosis involves intricate procedures, including image preprocessing, feature extraction, dimensionality reduction, feature evaluation, and classification. Typically, MRI-based methods for AD assessment focus on two primary components: feature extraction from MRI images and classifiers that utilize these extracted features. Popular classifiers used for this purpose include Bayesian classifiers, logistic regression, neural networks such as Support Vector Machines (SVMs), random forests, and discriminating analyses.

Feature extraction, a crucial process in MRI analysis, can be divided into three approaches: voxel-based, region of interest (ROI)-based, and patch-based methods. These techniques focus on quantifying features like the volume, texture, or shape of brain structures. The selected features may come from various brain regions or specific patterns, with some studies concentrating on the hippocampus,

known for its association with memory and early-stage AD. Features might also be derived from sources such as grey matter, image similarities, topologies, or higher-order derivatives from the original images.

Voxel-based approaches involve analyzing MRI data at a fine-grained level, allowing for detailed comparisons across different brain regions. ROI-based methods, on the other hand, concentrate on predefined brain regions, such as the hippocampus, which is most affected during AD progression. Patch-based techniques divide the brain into smaller regions or "patches" for more localized feature extraction, enabling the detection of subtle changes in brain structure. By applying these techniques, researchers aim to differentiate between healthy controls and individuals with AD, particularly in the early stages when intervention could yield significant clinical benefits.

Recent developments in deep learning, particularly convolutional neural networks (CNNs), have further improved the accuracy of AD detection. For instance, AlzheimerNet, a CNN classifier, was specifically developed to detect AD by analyzing MRI scans. AlzheimerNet outperformed other existing models, achieving an impressive test accuracy of 98.67% in identifying advanced stages of Alzheimer's disease. This model's success highlights the potential of CNNs in advancing AD diagnostics. Additionally, when compared with other state-of-the-art methods, AlzheimerNet's superior performance underscores the effectiveness of deep learning approaches in this domain.

Feature extraction in AD diagnosis is not limited to CNN-based models. Researchers have explored other techniques, including using voxel-based, ROI-based, and patch-based approaches to extract features from MRI scans. Shape, texture, and volume are properties that can be quantified through these techniques, providing critical insights into brain morphology changes associated with AD. Features extracted from grey matter or the hippocampus are particularly informative, as these regions undergo significant changes during the early stages of the disease. Furthermore, image similarities and topological features are also used to assess the degree of brain degeneration.

The application of ML in AD diagnosis also extends to feature selection and dimensionality reduction, which are vital for optimizing classifier performance. Dimensionality reduction techniques, such as principal component analysis (PCA), help condense large datasets, making them more manageable while retaining essential information. Reducing the number of features helps mitigate overfitting and improves the classifier's ability to generalize to new data.

Once the features are extracted and reduced, they are fed into classifiers for diagnosis. Neural networks, SVMs, and logistic regression are among the popular classifiers used to distinguish between healthy individuals and those with AD. These classifiers are trained using labeled data to identify patterns associated with different stages of the disease. The accuracy of these classifiers is crucial for early detection, which is essential for timely intervention and treatment.

The potential benefits of AI in early AD detection extend beyond diagnosis. For patients and caregivers, an early and accurate diagnosis can reduce anxiety and provide clarity on treatment options. For instance, early intervention can delay the disease's progression, improving the patient's quality of life. Moreover, early detection can reduce healthcare costs by minimizing the need for more extensive treatments in later stages of the disease.

The process of training AI models for AD diagnosis, however, comes with challenges. One significant limitation is the reliance on large, well-labeled datasets. Models like AlzheimerNet require extensive data for training, which may not always be readily available. Additionally, long training periods can reduce the efficiency of these models in real-world clinical settings. Data standardization is another issue, as inconsistencies in data acquisition and preprocessing can affect model performance. Overcoming these challenges requires improved data collection practices and the development of more efficient models that can operate with smaller datasets.

In the context of data processing, convolutional layers are widely used to extract spatial information through down-sampling and convolutions. After feature extraction, transformers can be employed to process these local features, breaking down visual data into smaller, more manageable components. This process, known as patching, allows the model to focus on local and global features, improving its ability to detect subtle changes in brain structure. Self-attention mechanisms, often used in transformers, further enhance the model's capacity to learn relationships between different patches, allowing for more accurate classification.

The self-attention process relies on covariance matrices to normalize the attention scores, ensuring gradient stability during training. This regularization technique, known as stochastic depth, helps prevent overfitting and makes deep neural networks more applicable to real-world scenarios. The combination of convolutional layers, transformers, and self-attention mechanisms has proven effective in capturing both local and global features, enhancing the model's ability to detect AD with high accuracy.

Finally, data normalization and handling of missing data points are critical steps in ensuring optimal model performance. AI models often require consistent and complete data for training. Missing data can be addressed through statistical imputation methods or removed if they do not significantly impact the overall dataset. Data normalization, which adjusts data points to a consistent scale, is also essential for improving classifier performance.

AI and ML have shown immense promise in detecting Alzheimer's disease using structural MRI. By automating the process of feature extraction, dimensionality reduction, and classification, AI systems can provide more accurate and timely diagnoses. While challenges

like data availability and model efficiency remain, continued advancements in deep learning and image processing techniques are expected to overcome these hurdles. The integration of AI into the diagnostic process for neurodegenerative diseases like AD represents a significant step forward in improving patient outcomes and reducing healthcare costs.

AI model

We have developed an AI model below (**Figure 1**).

The input pictures I_x and their corresponding labels are the starting points. With the help of data enhancement techniques, researchers can get improved copies of the data, which are represented as I'_x. The approach begins by reducing and normalizing the data because of the restricted computing resources. The photos are thus reduced in size to 128 × 128. The variables I'_{min} and I'_{max} Indicate the lowest and highest values for each occurrence after the augmentation phase. The data instance I''_x is the outcome of the data augmentation, resizing, and scaling processes, as shown in Equation 1.

$$I''_x = \frac{I'_x - I'_{min}}{I'_{max} - I'_{min}} \quad (1)$$

In processes that follow initial pre-processing, the whole picture is split into 256 smaller patches, with dimensions 8×8×3, during the patching procedure. These patches are then projected onto an area with lower dimensions. Equation 2 contains the mathematical method for applying patches to the data batch. In Equation 2, the patches of a single instance are represented by I''^X_x, where X ranges from 1 to the number of patches, and K stands for the learnable embeddings.

$$S_m = [I_{class}; I''^1_x K; I''^2_x K \ldots . I''^X_x K] + K_{pos} \quad (2)$$

Data processing uses convolutional layers, which extract spatial information by using down sampling and convolutions. After that, the transformer receives these present tokens representing these local characteristics and processes them further. It breaks down the visual data into smaller pieces, as seen in Equations 3 and 4.

$$G_x = MaxPool(ReLU(Conv2d(I''_x))) \quad (3)$$

$$S_l = [i_{class}; G''^1_x K; G''^2_x K \ldots . G''^X_x K] + K_{pos} \quad (4)$$

Using 8×8×3 patches in the patching module and 16×16×3 patches in the tokenization module, the location and channel knowledge offered by the images is successfully collected and represented. Larger token sizes capture a wider context, while smaller patch sizes allow for gathering more precise information; this enables the accomplishment of both global and specific context elements via the utilization of varied sizes. This enhanced data is useful for both attention systems because it facilitates the learning of local and global subtle features. The model learns the relationships between patched and tokens via self-attention, which helps it comprehend the picture's environmental data and spatial connections. Equations 5 and 6 are the mathematical expressions for the self-attention process in classification time that is used with S_m and S_l.

$$Attention(S_m, S_m, S_l) = Softmax\left(\frac{S_m S_m^L}{\sqrt{E_p}}\right).S_l \quad (5)$$

The covariance matrix, denoted as ϕ, substitutes for the matrix product $S_m S_m^L$. In self-attention, the dot product attention ratings are normalized using $\sqrt{E_p}$ as a scale factor, maintaining gradient stability throughout training is aided by this.

$$Attention(S_l, S_l, S_m) = Softmax\left(\frac{S_l S_l^L}{\sqrt{E_p}}\right).S_m \quad (6)$$

The covariance matrix, denoted by Ψ, substitutes for the matrix product $S_l S_l^L$. During training, stochastic depth is a method for haphazardly removing or skipping network layers. This regularisation approach aims to make deep neural networks more effective and applicable in real-world scenarios. One can see the application of stochastic depth to Equation 7 in Equation 8. Stochastic depth is based on the drop probability ϖ, and the maintain probability is 1 minus ϱ. Equation 7 describes the mathematical form of probability called keep probability.

$$\varrho = 1 - \varpi \quad (7)$$

Equation 8 shows the $\mathcal{W}_\delta$ vector, which is produced from a random distribution.

$$\mathcal{W}_\delta = (\varrho + \mathcal{W}_\Theta)\epsilon\mathcal{B} \quad (8)$$

The uniform vector $\mathcal{W}_\Theta$ Equation 8 is chosen from a simple random distribution ranging from 0 to 1. It transforms the resultant vector values into integers inside the domain $\mathcal{B}$ by using the floor function after adding ϱ. Equation 9 shows the output that is generated after applying stochastic depth.

$$R_{db} = \frac{\mathcal{W}_\delta}{\varrho}.Softmax\left(\frac{\Psi}{\sqrt{E_p}}\right).S_m \quad (9)$$

In the event of patching, the output of self-attention is subjected to the dense transformation and concatenation procedures, denoted by ω_θ, as outlined in Equation 10.

$$\omega_\theta = \omega_\theta\left(Softmax\left(\frac{\Phi}{\sqrt{E_p}}\right).S_l\right) \quad (10)$$

As seen in Equation 11, self-attention output undergoes the same changes as transformation.

$$\omega_\Omega = \omega_\Omega\left(\frac{\mathcal{W}_\delta}{\varrho}.Softmax\left(\frac{\Psi}{\sqrt{E_p}}\right).S_m\right) \quad (11)$$

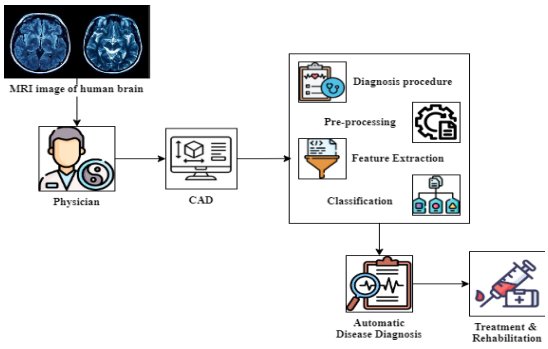

Figure 1. AI-based CAD for AD diagnostics.

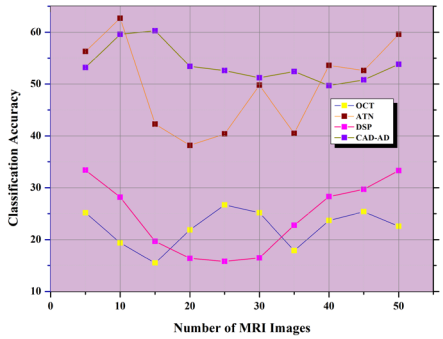

Figure 2a. Classification Accuracy.

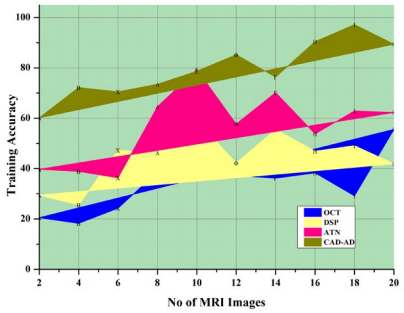

Figure 2b. Training Accuracy.

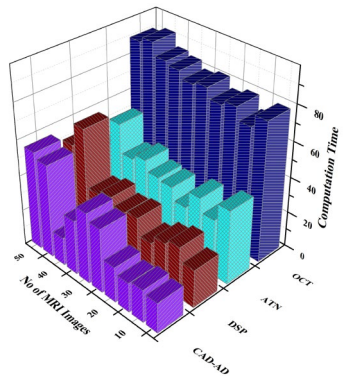

Figure 3a. Computation Time.

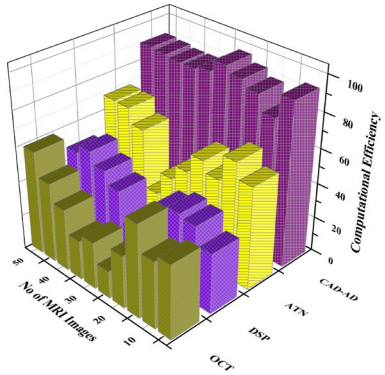

Figure 3b. Computation Efficiency.

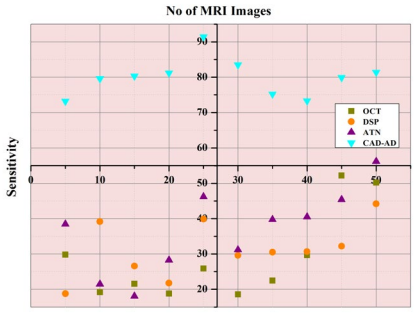

Figure 4a. Sensitivity ratio.

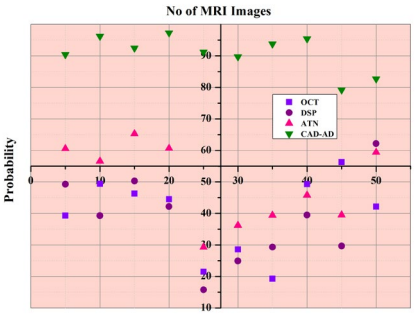

Figure 4b. Probability ratio.

Lastly, the representations ω and Ω are then compounded by the matrix representing their weights, as shown in Equations 12 and 13, and attention weights are obtained.

$$\omega_u = \eta(\omega_\theta . \xi_1)_x^L . \omega_\theta \quad (12)$$

The product of ω_θ and the trainable weight matrix ξ_1, represented as $\eta(\omega_\theta . \xi_1)_x^L$, are subjected to the softmax function η in Equation 12. When the weight matrix ξ is multiplied by the output (η), the soft-max function is applied, as shown by the formula $\eta(\omega_\theta . \xi_1)_x^L$. Likewise, the procedure outlined in Equation 13 is carried out during the concentration transmission step.

$$\Omega_u = \eta(\Omega_\theta . \xi_2)_x^L . \Omega_\theta \quad (13)$$

To merge the weighted representations produced, we integrate a fusion function, $\mathcal{H}_\tau$, at last. This fusion function combines both representations' data. The fusion technique used in a particular example is concatenation, as shown in Equation 14.

$$\mathcal{H}_\tau = \mathcal{H}_\tau(\omega_u, \Omega_u) \quad (14)$$

Two arguments, ω_u and u, are sent to the fusion function, represented as $\mathcal{H}$ fusion in Equation 15.

$$\mathcal{H}_\tau = \mathcal{H}_\tau(\eta(\omega_\theta . \xi_1)_x^L . \omega_\theta, \eta(\Omega_\theta . \xi_2)_x^L . \Omega_\theta) \quad (15)$$

The multiclass classification job necessitates using a Softmax classifier, and Equation 15 shows the final representations fed into this algorithm. The procedure is repeated n times to learn representations efficiently, beginning with self-attention and continuing until Equation 15. Encoding patches or tokens into meaningful representations is generally called transformer encoding.

Data points must be provided at regular intervals with no missing data points, even if optimal data is not essential for AI. There is a lack of data standardization throughout the data preparation phase. Assuming the data adhere to the asymmetry rule, the scenario may be fitted using predefined time points. In addition, statistical values should be used to replace missing data that is neither null nor a number. When there aren't enough data points or when the data are consistent, it's better to remove the variables to get better results. To enhance the performance metrics, it is necessary to normalize the data points based on their reference ranges.

Dataset Description

To train different machine learning models to detect patients with mild to moderate dementia, the team has discovered MRI-related data that the Scanning Research produced in an accessible Collection (OASIS) project. This data is accessible on both their website and Kaggle (Kaggle.com). About 150 people, aged 60 to 96 are included in the collection based on longitudinal magnetic resonance imaging data. At least once, every topic was scanned. 'Nondemented' was the treatment group for 72 of the participants. Sixty-four participants were initially classified as "Demented" and stayed in that category throughout the research. Fourteen individuals were initially classified as "Nondemented" but were later reclassified as "Demented" at a second evaluation. This group includes the 'Converted' items.

Classification Accuracy Vs Training Accuracy

The proportion of samples that were properly recognized was the accuracy statistic (Figure 2A, 2B). The following is Equation 16 for determining the binary classification's accuracy:

$$Accuracy = \left(\frac{TP+TN}{TP+TN+FP+FN}\right) \quad (16)$$

In Equation 16, where TP stands for correct optimistic instances work, TN for correct negative example projects, FP for incorrect positive example assignments to negative classes, and FN for incorrect negative instance responsibilities to certain classes.

Figures 4a and 4b show that this article outlines a method to drastically reduce pre-training time by using the 2D transfer network's pre-training significance to extract features. Compared to the standard 2D transfer network, AD diagnosis's time and classification accuracy are significantly improved. Traditional machine learning classification works better when finding things that can be used for data mining. Nevertheless, picture classification isn't always perfect; for example, AD has hazy symptoms. According to the experimental results, this research's methodology outperforms prior approaches in terms of classification accuracy.

Computation Time Vs Efficiency

Figure 3 shows that the study's transfer network, a machine learning approach for AD-assisted diagnosis, has several benefits, including reduced training time and improved computing efficiency. Using Equations 5 and 6, the overall time required to complete each transfer technique, the times spent extracting barrier attributes, the highest capabilities, and identifying the level. Furthermore, although previous research has used multimodal classification methods to obtain high accuracy, the study uses MRI data to classify AD. This article's transfer network outperforms state-of-the-art approaches regarding AD classification accuracy. Nevertheless, training will take much longer due to the weight rising significantly when CAD-AD directly feeds 3D MRI image data into the deep network. Furthermore, the execution time is significantly reduced, albeit the following aspects require further examination.

Sensitivity Vs Probability analysis

Find all positive samples where the classifier's activity is shown by sensitivity, also called recall and true positive rate. The sensitivity metric displays the proportion of AD patients whose diagnoses were accurately determined relative to the total AD patients. Here is Equation 17 for determining sensitivity:

$$Sensitivity = \frac{TP}{TP+FN} \quad (17)$$

Figure 4a shows that it is evident that the suggested strategy much surpasses the alternatives in three different categorization tasks. Also, while comparing CAD-AD vs. OCT, DSP, and ATN, the suggested technique attained 81.4%, respectively. In addition,

compared to traditional methodologies, our suggested approach had the maximum sensitivity across all tasks, suggesting that it may significantly improve the ability to distinguish between AD. Therefore, the suggested method can correctly identify individuals with AD compared to the approaches mentioned. Reasons for this performance include the suggested method's efficacy in merging multimodal data and its capacity to learn the high-level features from all samples in the provided dataset.

Despite CAD-AD's demonstrated efficiency in AD classification, the CAD-AD model offers a formidable alternative. Using a sigmoid function that takes values between 0 and 1, we may determine the ultimate probability that a sample belongs to a certain category. After the loss was defined, Equation 7 & 8 showed the probability ratio for each category. However, transformers also do very well in these domains; they use self-attention processes to spot intricate spatial patterns, which are crucial for accurate diagnosis. It might also be challenging to understand model decisions, which are essential in medical applications, because of the complex hierarchical topologies of CNNs. Conversely, the attention processes of transformers allow for better interpretability and transparency in decision-making.

5. Discussion and Conclusion

Neurodegenerative disorders (NDDs) are characterized by the gradual loss of neurons due to a complex interplay of environmental, pharmacological, genetic, and epigenetic factors. The degeneration of oxidoreductase activity and antioxidant systems leads to the production of free radicals, which promote the aggregation of misfolded proteins within the central nervous system (CNS). This aggregation results in neuroinflammation, metabolic disturbances, and ultimately contributes to the onset of NDDs.

Diagnosis of neurodegenerative diseases typically involves quantifying specific receptor binding, assessing changes in cellular metabolism, and identifying structural abnormalities. Neuroimaging techniques, particularly magnetic resonance imaging (MRI), play a crucial role in elucidating the metabolic fate of damaged neuronal cells and evaluating their receptor activity. A relatively novel approach in the diagnosis and prognosis of NDDs is metabolomics, which analyzes metabolic changes in the body that may indicate disease progression.

Additionally, this review highlights the regulatory role of angiogenesis in various tumor hallmarks and its significant involvement in pathological changes associated with malignancy, including tumor formation, proliferation, and metastasis. Various antiangiogenic therapies, such as monoclonal antibodies, small molecule inhibitors, angiostatin, endostatin, and melatonin analogues, have been developed to inhibit angiogenesis by modulating the expression of angiogenic biomarkers. Targeting the angiogenic process is particularly promising, as it deprives tumors of the blood supply essential for their growth.

To further explore the therapeutic potential of these antiangiogenic agents in treating conditions like Alzheimer's disease, there is a pressing need for network-based investigations and advanced artificial intelligence (AI) processing.

Accessible and timely medical treatment is essential for public health, and Computer-Aided Diagnosis (CAD) systems play a vital role in enhancing diagnostic efficiency and accuracy in medical imaging. CAD technology significantly improves the speed of disease detection, consistently performing well regardless of the operator's experience, thereby mitigating the risk of human error. However, while the development of CAD systems presents numerous advantages, it also poses challenges that require collaboration among patients, healthcare professionals, and pharmaceutical stakeholders to address.

The integration of CAD systems with imaging modalities such as digital mammography, computed tomography (CT), and MRI is on the horizon, offering the potential to identify a range of diseases and lesions. Routine clinical diagnostics represent another area where CAD can significantly contribute. Future research is expected to delve into various avenues, including the application of AI in image-based CAD, tailored treatments, remote diagnostics, and real-time assessments. The rise of telemedicine facilitates the adaptation of CAD systems for remote diagnosis, enhancing accessibility to care.

In the coming years, CAD systems may evolve to synthesize data from X-rays, MRIs, CT scans, and digital medical records alongside non-imaging data. This integrated approach has the potential to personalize diagnosis and treatment based on a patient's unique genetic profile, medical history, and lifestyle factors. Ultimately, the integration of knowledge from both clinical and technical fields will be critical for the advancement of CAD systems, leading to improved outcomes in patient care.

Author contributions

S.A. designed methodology and wrote draft. G. S. validated and conceptualized the study. B.J. interpreted the data. M. J.D. E. data collection and analysis. B. V. V. wrote. S.S. reviewed, edited the article.

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Competing financial interests

The authors have no conflict of interest.

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