A DEEP LEARNING APPROACH WITH GRAPH NEURAL NETWORKS FOR UNVEILING AD PATHOLOGY THROUGH MRI BIO MARKERS

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ABSTRACT

Alzheimer's disease is a progressive neurodegenerative disorder that significantly impacts cognitive function, making early and accurate diagnosis crucial. In this study, we propose an Alzheimer's Disease Graph Neural Network (AD-GNN) to classify MRI brain images into five categories: Alzheimer's Disease (AD), Cognitive Normal (CN), Early Mild Cognitive Impairment (EMCI), Late Mild Cognitive Impairment (LMCI), and Mild Cognitive Impairment (MCI). The model transforms MRI data into a graph structure, where each pixel represents a node, and edges between neighboring nodes capture local anatomical connectivity.

A key advantage of graph-based learning is its ability to capture the underlying structural and relational information within brain regions. By treating the brain as a graph, the model can analyze complex spatial relationships, making it particularly effective in recognizing subtle changes in brain connectivity that are critical for diagnosing different stages of Alzheimer's disease, enhancing the prediction accuracy. Experimental results demonstrate that AD-GNN effectively distinguishes between different stages of Alzheimer's and cognitive states. Overall, this research offers a promising solution for earlier and more accurate AD detection, with potential benefits for patient care and research in neurodegenerative diseases.

Keywords: Alzheimer's Disease, GNN, CN, EMCI, LMCI, MCI

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I. INTRODUCTION

As life expectancy steadily climbs, Alzheimer's disease, a progressive neuro degenerative disorder, becomes a growing threat to our aging population. This insidious disease, characterized by the gradual erosion of cognitive function and memory is caused by the brain accumulating abnormal proteins, with beta-amyloid forming plaques and tau tangling inside nerve cells. Age is the biggest risk factor, although genetics, head injuries, and poor cardiovascular health may also contribute. This process disrupts communication between brain cells, leading to their death and the characteristic memory decline and cognitive issues of Alzheimer's. Early and accurate diagnosis of AD is paramount in this battle. It allows for the timely implementation of treatment plans that can slow the progression of symptoms, improve the quality of life for patients, and alleviate the immense burden placed on care givers and healthcare systems.

Traditional methods for diagnosing AD often rely on a battery of cognitive assessments, a series of tests designed to evaluate an individual's memory, thinking, and reasoning skills. While these assessments can provide valuable insights, they are susceptible to limitations. Firstly, cognitive assessments can be subjective, depending on the interviewer's interpretation and the patient's performance on a given day. Secondly, the administration of these tests can be time-consuming, further straining already limited resources. Perhaps most critically, in the early stages of AD, cognitive decline may be subtle and easily dismissed as a normal part of aging. This makes timely detection using traditional methods a significant challenge.

Furthermore, while some diagnostic procedures for Alzheimer's disease, such as lumbar punctures to analyze cerebrospinal fluid, offer valuable insights, they can be invasive and pose risks of complications, highlighting the need for less invasive alternatives. Neuroimaging techniques like MRI and PET scans present non-invasive options that provide valuable information without the associated

discomfort and risks. MRI scans can visualize brain shrinkage in AD-related areas, while PET scans can detect protein buildup characteristic of the disease. These techniques offer valuable insights into AD pathology while minimizing patient discomfort and risk.

In recent years, advancements in medical imaging have opened new avenues for exploring alternative diagnostic techniques for AD. Deep learning (DL), a subfield of artificial intelligence, has revolutionized the analysis of medical images. DL algorithms, trained on extensive datasets of brain scans, have demonstrated promising results in AD detection. These algorithms can be likened to highly skilled detectives, meticulously sifting through vast amounts of data to identify subtle patterns and abnormalities in brain structure that may be indicative of AD. They can learn to recognize the telltale signs of the disease, such as shrinkage in specific brain regions or the accumulation of abnormal proteins.

However, despite the immense potential of DL, it's crucial to acknowledge its limitations. The accuracy of DL models heavily relies on the quality and size of the training datasets. Acquiring large, high-quality datasets can be expensive and time-consuming. Furthermore, DL models can be considered black boxes, their internal decision-making processes are often opaque, making it difficult to understand how they arrive at their predictions. This lack of interpretability can limit the clinical utility of DL models in certain settings. Clinicians may be hesitant to rely solely on a black box for such a critical diagnosis.

Moreover, the complex interplay of factors underlying AD goes beyond purely structural changes in the brain. Genetic predisposition, environmental factors like exposure to pollutants or head injuries, and other biological processes all play a role in the development and progression of the disease. DL models, while powerful for image analysis, may not fully capture this intricate interplay. They may excel at identifying patterns in brain scans, but they may struggle to integrate this information with a broader understanding of the disease's underlying biology.

This research proposes a novel approach to address these challenges, which involves combining hybrid deep learning with targeted anatomical biomarkers. By strategically integrating domain knowledge of relevant anatomical changes associated with AD into the DL framework aiming to achieve a more robust and informative diagnostic tool, leveraging the strengths of both the ability of DL to identify complex patterns in brain scans and the specificity of anatomical biomarkers in pinpointing disease-related changes. Biomarkers can be thought of as specific biological signatures of the disease, such as the levels of certain proteins in the cerebrospinal fluid or specific changes in brain tissue composition. These biomarkers provide valuable insights into disease processes.

This hybrid approach not only enhances the accuracy and efficiency of AD detection but also paves the way for earlier diagnosis, better patient outcomes, and a brighter future in the fight against Alzheimer's disease. By combining the strengths of deep learning's pattern recognition and the specificity of anatomical biomarkers, this approach creates a more comprehensive and reliable diagnostic tool that can empower clinicians to make informed decisions about patient care.

II. LITERATURE SURVEY

Ahmed, H.M., et. al., 2023 [1] proposed a DCNN framework for Alzheimer's diagnosis using brain MRI scans, classifying Normal Controls (NC), Mild Cognitive Impairment (MCI), and AD. Using the ADNI dataset, the model achieved 100% accuracy for AD/NC, 92.93% for NC/MCI, and 99.21% for AD/MCI, with an overall accuracy of 93.86%. ROC analysis showed AUC values of 1 for AD and NC, and 0.989 for MCI, outperforming prior studies. Arya, A.D., et. al., 2023 [2] described Alzheimer's disease as a progressive, incurable condition, where early and accurate diagnosis is crucial to predict whether patients with mild cognitive impairment (MCI) will develop AD. The study emphasized PET and MRI imaging techniques, and reviewed the use of machine learning and deep learning for early classification of normal cognitive (NC) and AD patients, assessing their performance across various classifiers. Ávila-

Jiménez, J.L., et. al., 2024 [3] developed a Deep Learning model to classify dementia patients with Alzheimer's disease using clinical data. The dataset was preprocessed with rebalancing techniques, and the model was optimized through several studies. It outperformed established machine learning methods, achieving superior AUC performance with a significance level below 0.05, proving to be an effective tool for AD diagnosis.

Bamber, S.S., et. al., 2023 [4] highlighted the importance of medical image classification in Alzheimer's disease diagnosis and research, a major cause of dementia in the elderly. Traditional methods faced limitations in accuracy and required extensive feature extraction. To address this, the researchers developed a deep neural network with a shallow convolutional layer, designed to be both highly accurate and interpretable for medical professionals. The model achieved approximately 98% accuracy, surpassing existing approaches and showing promise for improving early diagnosis and reducing Alzheimer's-related mortality. Eslami, M., et. al., 2023 [5] tackled the persistent challenge of automating the diagnosis and prognosis of Alzheimer's disease through ML techniques. They presented a novel method featuring a color-coded visualization mechanism driven by an integrated ML model to predict disease progression over a 2-year longitudinal study. The main objective was to improve understanding of AD processes using 2D and 3D renderings, facilitating both multiclass classification and regression analysis. This innovative approach offered a visual means to monitor AD trajectory, providing valuable insights into the progression of the disease.

Gnanadesigan, N.S., et. al., 2023 [6] explored Alzheimer's disease, a neurological condition associated with memory loss, emphasizing the absence of effective treatments and the unclear causes of the disease. They introduced a novel Degree Centrality-Graph Colouring (DC-GC) model, which attained an impressive 96% accuracy using the Artificial Neural Network (ANN) classifier, along with strong sensitivity and specificity results. By combining advanced machine learning models with network topology measures, the research enhanced the identification of candidate genes related to AD, providing valuable insights for potential therapeutic targets. Hu, Z., et. al., 2023 [7] explored mild cognitive impairment (MCI) as a critical transitional stage between normal aging and Alzheimer's disease, highlighting the necessity of accurately predicting MCI progression for timely intervention. They introduced the VGG-TSwinformer model, which combines convolutional neural networks (CNN) and Transformer techniques to analyze longitudinal structural MRI data. When validated on the ADNI dataset, the model showed enhanced accuracy, sensitivity, specificity, and AUC compared to existing cross-sectional studies, thereby improving diagnostic efficiency by effectively modeling brain atrophy progression from longitudinal MRI images. Illakiya, T., et. al., 2023 [8] conducted a comprehensive review, analysing 103 research articles exploring the potential of deep learning for Alzheimer's disease detection using neuroimaging modalities like MRI and Positron Emission Tomography (PET). Their analysis focused on various deep learning techniques such as CNNs, Recurrent Neural Networks (RNNs) and Transfer Learning (TL). This review highlighted the promising results achieved in AD detection using these methods.

Leela, M., et. al., 2023 [9] proposed Hybrid EEG and Fused CT-MRI based RPCA integrated Deep Transfer Learning (HEMRDTL) model, combining data from electroencephalogram (EEG) and fused CT-MRI scans for early Alzheimer's detection. It utilized transfer learning, deep Visual Geometry Group -19 techniques (VGG) and Robust Principal Component Analysis (RPCA) for feature extraction and classification. Marwa, E.G., et. al., 2023 [10] proposed a precise AD detection method using MRI scans. This method utilized a shallow CNN and 2D T1- weighted Magnetic Resonance (MR) images, achieving exceptional accuracy of 99.68% in classifying AD stages, including stratification of Mild Cognitive Impairment (MCI) into various dementia stages.Nour, M., et. al., 2024 [11] highlighted the use of AI in diagnosing Alzheimer's disease and dementia but noted challenges in distinguishing AD from Healthy Controls (HC) using EEG signals. The study proposed a Deep Ensemble Learning (DEL) approach with 2D-CNN, achieving 97.9% accuracy in AD classification without prior feature extraction, showcasing the potential of

ensemble learning for improving diagnostic tools.

Odusami, M., et. al., 2023 [12] introduced an innovative heuristic early feature fusion framework that integrated PET and MRI data to enhance early detection of Alzheimer's disease. By employing a modified Resnet18 architecture, the model achieved a classification accuracy of 73.90% on the ADNI database, effectively tackling data heterogeneity and offering an Explainable Artificial Intelligence (XAI) model for interpreting results. Park, H.Y., et. al., 2023 [13] proposed an automatic Alzheimer's disease and MCI classification algorithm using TabNet,an interpretable model, compared with Xtreme Gradient Boosting (XGBoost) using brain scans. Both achieved similar accuracy, but TabNet offers interpretability of brain regions. Radiomics data didn't improve TabNet's performance.Rahim, N., et. al., 2023 [14] proposed a hybrid multimodal deep-learning framework combining 3D CNN and Bidirectional Recurrent Neural Network (BRNN) models for early AD detection using longitudinal MRI scans. This model integrated biomarkers for better accuracy offering an explanation tool to aid doctors' interpretation.Rajesh Khanna, M., 2023 [15] proposed a method combining Deep Convolutional Neural Network (MobileNetV2) and deep ensemble learning (LSTM) to classify Alzheimer's disease stages using MRI images. This approach outperformed CNN, achieving high accuracy with 94% sensitivity and 95% specificity.

Rallabandi, V.S., et. al., 2023 [16] proposed an Inception-ResNet model for automated dementia staging by combining MRI and PET scans. Their approach demonstrated high accuracy in classifying healthy controls, MCI and Alzheimer's disease, suggesting promising for improved clinical diagnosis. Shigemizu, D., et. al., 2023 [17] examined the genetic architecture of late-onset Alzheimer's disease (LOAD) through Japanese GWAS data, revealing two distinct patient groups defined by risk genes. They developed a deep neural network prediction model for LOAD subtypes, achieving accuracies of 0.694 in the discovery cohort and 0.687 in the validation cohort, providing new insights into the disease's pathogenic mechanisms. Sudharsan, M., et. al., 2023 [18] proposed an early Alzheimer's diagnosis method using Mild Cognitive Impairment (MCI) and Structural Magnetic Resonance Imaging (sMRI). This method employed three classifiers which are Import Vector Machine (IVM), Regularized Extreme Learning Machine (RELM) and Support Vector Machine (SVM). The results from the Alzheimer's disease Neuroimaging Initiative (ADNI) datasets showed that Regularized Extreme Learning Machines (RELM) significantly improved the classification accuracy.

Thangavel, P., et. al., 2023 [19] proposed an Early Alzheimer's disease prediction using Deep Neural Networks (EAD-DNN) utilizing Magnetic Resonance Imaging (MRI) datasets. CNN and ResNet were used to extract crucial information from brain scans, while optimized Adam refines data. This multi-class approach achieved a reported 98% accuracy. Yao, Z., et. al., 2023 [20] presented Fuzzy-VGG, a novel approach that enhances Alzheimer's disease classification by prioritizing image quality. Using fuzzy theory to reorder pixels and a two-stage cutout for data augmentation, the method improved classification and model convergence. The study emphasized local key areas for training and introduced blockchain for scalability and continuous improvement.

The aim of this research is to develop and assess an innovative deep learning architecture, the Alzheimer's disease Graph Neural Network (AD-GNN), designed to enhance the classification of MRI images for detecting Alzheimer's disease. This study leverages a graph-based approach to analyze the brain's structural and connectivity patterns, addressing challenges such as image variability and the subtle nuances of cognitive impairment. By transforming MRI scans into graph structures, the research seeks to demonstrate that AD-GNN significantly improves classification accuracy over existing methods, ultimately providing a more effective tool for diagnosing Alzheimer's disease. The key contributions are:

- The graph-based representation of MRI images enables the model to capture local anatomical relationships, enhancing its ability to distinguish between Alzheimer's disease and other cognitive states.

- The architecture integrates multiple graph convolutional layers, which progressively extract deeper graph-based features, thereby improving robustness and accuracy in classification.

This paper is organized into five sections. The introduction defines Alzheimer's disease, explores its symptoms, and highlights the urgent need for improved diagnostic tools. It introduces the Alzheimer's disease Graph Neural Network, a novel deep learning architecture designed to enhance classification from MRI images by addressing challenges like image variability and subtle cognitive changes. The literature review examines recent research and existing methods for Alzheimer's disease detection using MRI, discussing the limitations of current approaches and the need for advanced models. The methodology section details the preprocessing steps, including resizing, Z-score normalization, non-local means filtering, unsharp masking, and skull stripping. It also describes the graph structure, graph convolutional layers, and the training process, including loss functions and evaluation metrics. In the results and analysis section, experimental results are presented, demonstrating the model's superior performance compared to other methods. This analysis includes strengths, limitations, and performance metrics. Finally, the conclusion summarizes the key findings, evaluates the model's effectiveness, and suggests areas for future research and potential improvements to enhance diagnostic accuracy.

III. METHODOLOGY

During the classification of MRI scans for detecting Alzheimer's disease, the raw images go through a series of important preprocessing steps. Initially, the scans are resized to achieve a consistent resolution. Next, Z-score normalization is applied to standardize the intensity levels.

by unsharp masking to sharpen the image edges for better clarity. Skull stripping is then employed to eliminate non-brain tissues, resulting in a refined brain image. This preprocessed image is then fed into the AD-GNN, which examines the brain's structure and connectivity to categorize the subject as either healthy or affected by Alzheimer's disease.

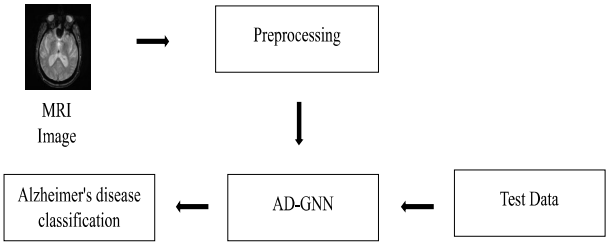


Figure 1: Flowchart of Alzheimer's Disease Classification

Figure 1 illustrates the flowchart for classifying Alzheimer's disease using a Graph Neural Network, beginning with MRI brain image acquisition and preprocessing. The processed images are transformed into a graph format, enabling the AD-GNN to identify cognitive states and categorize them.

3.1 PREPROCESSING

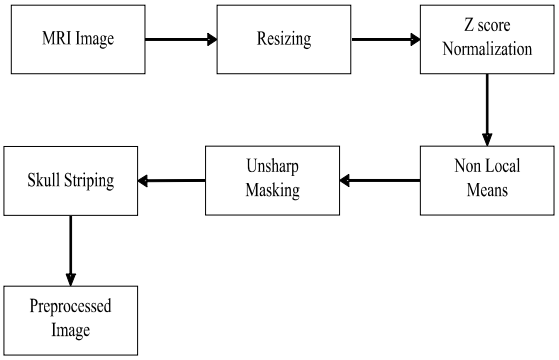


Figure 2: Preprocessing Pipeline for MRI Images

Figure 2 illustrates the preprocessing pipeline for MRI images, involving steps such as resizing to standard dimensions, Z-score normalization to adjust image intensity distribution, non-local means denoising for noise reduction, unsharp masking to enhance image contrast, and skull stripping to isolate brain tissue, resulting in the final preprocessed image.

3.1.1 RESIZING

To ensure uniformity and compatibility with downstream analysis and machine learning models, the MRI brain images were resized to a standard shape of 128x128 pixels. This resizing process is crucial for maintaining a consistent input size across all images, simplifying computational workflows and enhancing the performance of deep learning models, which typically require fixed input dimensions.

3.1.2 Z-SCORE NORMALIZATION

The resized MRI brain images were standardized using Z-score normalization to bring intensity values across all scans to a common scale. This method allowed for consistent comparison of pixel intensities both within individual scans and across different subjects. The normalization process applied the formula:

$$x' = \frac{x - \mu}{\sigma} \quad (1)$$

where x represents the original pixel intensity, μ is the mean intensity, and σ is the standard deviation of the intensities within the scan. As a result, the pixel intensities were transformed to have a mean of 0 and a standard deviation of 1. This adjustment minimized the effects of variations in image acquisition and anatomical differences, ensuring that the intensity values were comparable across images. The normalized images enhanced the robustness and precision of the subsequent quantitative and statistical analyses.

3.1.3 NON-LOCAL MEANS (NLM)

The normalized MRI brain images were denoised using the non-local means algorithm to enhance image quality while preserving crucial anatomical details. NLM operates by computing a weighted average of similar patches, where the weights depend on the similarity between patches. Mathematically, for a pixel $x(i)$, its new intensity value $NL(x(i))$ is computed as:

$$NL(x(i)) = \sum_{j\omega\Omega} w(i,j)x(j) \quad (2)$$

where x(j) are pixel in the search window Ω, and w(i, j) are the weights assigned based on the similarity between pixel x(i) and x(j). The weights are given by:

$$w(i,j) = \frac{1}{z(i)} \exp\left(-\frac{\left||x(i) - x(j)|\right|^2}{h^2}\right) \quad (3)$$

where Z(i) is a normalization factor, and h is a filtering parameter controlling the degree of smoothing. This method leveraged the redundancy in the image to suppress noise while preserving important edges and details, resulting in cleaner images suitable for further analysis.

3.1.4 UNSHARP MASKING

After denoising the MRI images with the NLM algorithm, Unsharp Masking was applied to enhance the sharpness and highlight finer details. This technique involved subtracting a blurred version of the denoised image I_b from the original denoised image I_d, producing a mask:

$$M = I_d - I_b \quad (4)$$

The mask was then scaled by a sharpening factor k, and added back to the original denoised image to produce the final sharpened image I_s:

$$I_s = I_d + kM \quad (5)$$

This process accentuated high-frequency components (edges and details), resulting in a sharpened image with better visibility of anatomical structures for subsequent analysis.

3.1.5 BRAIN AREA SEGMENTATION

The subprocess library was employed to automate skull stripping, which is critical for isolating brain tissue from non-brain structures (skull, scalp). Skull stripping was performed using FSL's BET (Brain Extraction Tool), controlled via the subprocess module in python. Parameters such as input file paths, output directories, and specific BET options were handled programmatically, ensuring reproducibility. The processed images with accurately stripped skulls were essential for Alzheimer's disease classification.

3.2 ALZHEIMER'S DISEASE GRAPH NEURAL NETWORK

To categorize cognitive impairment and Alzheimer's disease using AD-GNN, the preprocessed 2D MRI brain images were transformed into a graph structure where each pixel within the preprocessed images was treated as a node in the graph. The spatial relationships between these pixels were established by creating edges that connected neighboring nodes in the up, down, left, and right directions, effectively representing the local anatomical structures of the brain. This approach enabled the capture of connectivity patterns and relationships inherent in the brain's architecture. By examining the 2D grid structure of the MRI image and connecting adjacent pixels, the graph structure allowed for the integration of graph-based techniques, facilitating the analysis of complex interactions among brain regions. Once the graph, consisting of nodes (pixels) and edges (neighboring relationships), is constructed, it is passed as input to the AD-GNN. The AD-GNN then applies graph convolution operations over this structured data, leveraging the spatial relationships to learn meaningful patterns. This enhances the model's ability to classify cognitive impairments based on the underlying connectivity patterns present in the MRI scans. The AD-GNN architecture featured several layers: an input layer followed by three graph convolutional layers (GCN). Each GCN layer is represented by the following equation:

$$H^{(l+1)} = \sigma\left(D^{-\frac{1}{2}}AD^{-\frac{1}{2}}H^{(l)}W^{(l)}\right) \quad (6)$$

where $H^{(l+1)}$ is the feature matrix at layer l, A is the adjacency matrix, D is the degree matrix, $W^{(l)}$ is the learnable weight matrix at layer l, andis the ReLU activation function. The first GCN layer had 64 filters, the second had 128 filters, and the third used 256 filters. After the graph convolutional layers, a global average pooling layer reduced the node-level features to a graph-level feature vector. The graph-level features were passed through two fully connected layers:

$$z = \sigma\left(W_f c^{(1)} h + b^{(1)}\right) \quad (7)$$

$$y = softmax\left(W_f c^{(2)} h + b^{(2)}\right) \quad (8)$$

The final layer, with 5 neurons, classified the images into AD, Cognitive Normal (CN), Early Mild Cognitive Impairment (EMCI), Late Mild Cognitive Impairment (LMCI), and Mild Cognitive Impairment (MCI). The model was trained using the adam optimizer with a learning rate of 0.001 over 100 epochs, optimizing the cross-entropy loss function:

$$L = -\sum_{c=1}^{c} y_c \log(\check{y}_c) \quad (9)$$

where y_c is the true label and $\check{y}_c$ is the predicted probability for class c. The AD-GNN effectively learned and distinguished cognitive states based on structural brain connectivity patterns.

3.7 ALZHEIMER'S DISEASE CLASSIFICATION

In this work, Alzheimer's disease classification was performed using AD-GNN model, which transformed preprocessed MRI brain images into graph structures. Each pixel within the brain was represented as a node, with edges connecting spatially adjacent pixels to reflect local anatomical relationships. The AD-GNN architecture comprised three graph convolutional layers, progressively capturing deeper graph-based features. These layers extracted spatial and structural patterns, followed by a global average pooling layer that condensed node-level features into a graph-level feature vector. This vector was processed by two fully connected layers, ultimately classifying the images into five categories: AD, CN, EMCI, LMCI and MCI. The model, optimized with the adam optimizer and a cross-entropy loss function, demonstrated the capability to distinguish between different cognitive states based on brain connectivity, facilitating accurate AD diagnosis. AD_GNN algorithm discusses all the steps involved in the Alzheimer's disease classification

Algorithm – AD_GNN ()

1. Preprocessing

1.1. Image Resizing:

Resize image I to a fixed size (128, 128):

$$I_{resized} = resize(I, (128,128))$$

1.2. Z-Score Normalization:

Normalize pixel intensities of $I_{resized}$:

$$I_{normalized}(x, y) = \frac{I_{resized}(x, y) - \mu}{\sigma}$$

where μ is the mean intensity and σ is the standard deviation.

1.3. Non-Local Means Denoising:

Apply non-local means denoising to enhance image quality:

$$I_{denoised} = NonLocalMeans(I_{normalized})$$

1.4. Unsharp Masking:

Apply unsharp masking to emphasize fine details:

$$I_{sharp} = I_{denoised} + k \cdot (I_{denoised} - Gaussianblur(I_{denoised}))$$

1.5. Skull Stripping:

Use FSL BET (via sub process) to perform skull stripping:

$$I_{brain} = BET(I_{sharp})$$

Output Image:

$$I_{pre} = I_{brain}$$

2. Model Architecture

2.1. Graph Construction:

- Convert the pre processed image I_{pre} into a graph representation G = (V, E), where each pixel is a node, and edges represent spatial relationships between neighboring pixels.

2.2. GNN Layers:

2.2.1. Graph Convolutional Layers:

- Apply the first GCN layer with filters W_1 and ReLU activation:

$$H_{gcn1} = \sigma\left(D^{-\frac{1}{2}}AD^{-\frac{1}{2}}H^{(0)}W_1\right)$$

where A is the adjacency matrix, D is the degree matrix, and $H^{(0)}$ is the input node feature matrix.

$$H_{gcn2} = \sigma\left(D^{-\frac{1}{2}}AD^{-\frac{1}{2}}H_{gcn1}W_1\right)$$

$$H_{gcn3} = \sigma\left(D^{-\frac{1}{2}}AD^{-\frac{1}{2}}H_{gcn2}W_1\right)$$

2.3. Global Average Pooling:

- Apply global average pooling to obtain graph-level features:

$$g = \frac{1}{|V|}\sum_{v \in V} H_v^{(3)}$$

2.4. Fully Connected Layers:

2.4.1. First Dense Layer:

- Apply a dense layer with ReLU activation:

$$H_{dense1} = \sigma(W_{dense1}g + b_{dense1})$$

$$H_{dense2} = \sigma(W_{dense2}H_{dense1} + b_{dense2})$$

2.5. Output Layer:

- Apply the final dense layer for classification with a softmax activation:

$$H_{output} = softmax(W_{out}H_{dense2} + b_{out})$$

Output:

Predicted class probabilities for Alzheimer's disease, Cognitive Normal, Early Mild Cognitive Impairment, Late Mild Cognitive Impairment, and Mild Cognitive Impairment.

3. Training

3.1. Loss Function:

- Use categorical cross-entropy loss to compute the discrepancy between predicted class probabilities $\check{y}_c$ and true labels y_c :

$$L = -\sum_{c=1}^{5} y_c \log(\check{y}_c)$$

3.2. Optimization:

- Update the model parameters using the Adam optimizer:

$$\theta_{new} = \theta - \eta \nabla_\theta L$$

where η is the learning rate, and $\nabla_\theta L$ is the gradient of the loss with respect to the model parameters θ

3.3. Iteration:

- Repeat training for a specified number of epochs until convergence.

4. Evaluation

4.1. Prediction on Test Data:

- Predict class probabilities for test images I_{test}

$$\hat{y}_{test} = Predict(I_{test}, \theta)$$

4.2. Performance Assessment:

- Assess model performance using accuracy, precision, recall, and F1 score.

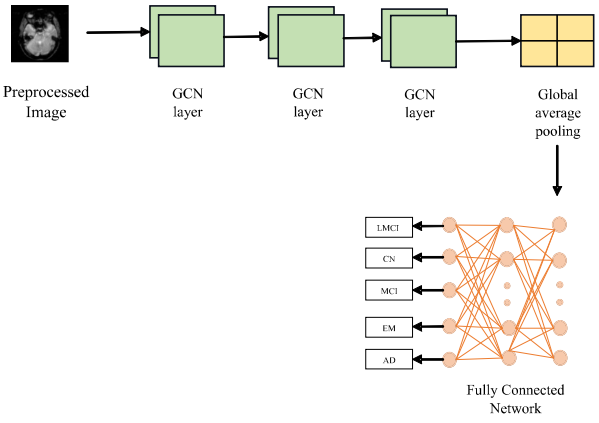


Figure 3: Architecture of the Proposed AD-GNN

Figure 3 depicts the architecture of the proposedAD-GNN for Alzheimer's disease classification. The input to the model is a preprocessed MRI image, which is passed through a series of three GCN layers that progressively learn spatial and structural features from the input data. Following the GCN layers, a Global Average Pooling layer is applied to reduce the spatial dimensions and aggregate the learned features globally. The pooled features are then fed into a fully connected network, which serves as the final classification layer, outputting the prediction for Alzheimer's disease. This architecture efficiently captures and processes complex image-based features for disease diagnosis.

IV. EXPERIMENT RESULT AND ANALYSIS

4.1 Dataset description

The dataset is intended for the classification of Alzheimer's disease and cognitive impairments using medical images. It comprises five categories: AD, CN, EMCI, LMCI, and MCI. The training set includes 7,536 images of AD, 7,430 images of CN, 240 images of EMCI, 72 images of LMCI, and 922 images of MCI. For evaluation, the test set contains 810 images of AD, 1,220 images of CN, 240 images of EMCI, 72 images of LMCI, and 233 images of MCI. This dataset provides a diverse collection of images to aid in the development and assessment of models for diagnosing and classifying different stages of cognitive impairment and Alzheimer's disease.

Table 1: Sample images of five classes

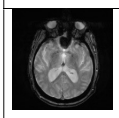
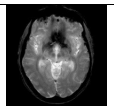
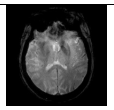
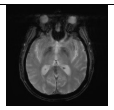
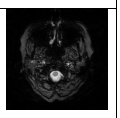
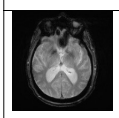
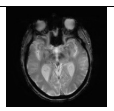
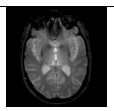
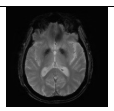
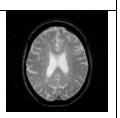
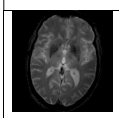
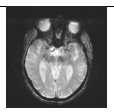
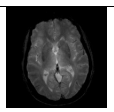
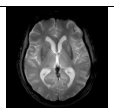
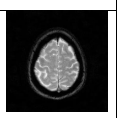
AD	CN	EMCI	LMCI	MCI
				
				
				

Table 1 displays sample images from five classes related to Alzheimer's disease classification: AD, CN, EMCI, LMCI and MCI. These images illustrate the morphological differences in brain MRI scans across stages, highlighting the structural variations that inform automated classification and enhance diagnostic accuracy for Alzheimer's disease.

4.2 Experimental Setup

The research was carried out on a workstation equipped with an Intel i5-4300U Processor clocked at 1.90 GHz, 8 GB of RAM, and a 64-bit operating system with x64-based architecture, running the Microsoft Windows 10 Pro operating system. Python implementation code was written using the Anaconda integrated development environment (IDE), with Tensor Flow and Keras libraries utilized for model implementation.

4.3 Result Analysis

The AD-GNN pipeline starts with preprocessing MRI brain images to prepare them for graph-based analysis. First, the images are resized to a uniform resolution, followed by Z-score normalization to standardize pixel intensity values across scans. Noise reduction is performed using the non-local means denoising technique, preserving key anatomical details. Unsharp masking is then applied to enhance image clarity by accentuating edges and fine structures. Skull stripping is conducted to remove non-brain tissues, isolating the brain for further analysis. The preprocessed images are then converted into graph structures, where each pixel is represented as a node, and edges are formed between adjacent pixel to capture local spatial relationships. These graph representations are subsequently fed into the AD-GNN model for classification. The model consists of three graph convolutional layers, which iteratively extract deeper spatial and structural features from the brain. A global average pooling layer follows, reducing the node-level features into a graph-level feature vector. This feature vector is then passed through two fully connected layers to classify the images into five categories: AD, CN, EMCI, LMCI and MCI. The model is trained using the Adam optimizer with a cross-entropy loss function to accurately diagnose alzheimer's based on brain connectivity patterns.

In classification tasks, key performance metrics such as accuracy, sensitivity, specificity, precision, and the F1 score are essential for evaluating model effectiveness. Accuracy measures the overall correctness of the model, while sensitivity focuses on its ability to correctly identify positive cases. Specificity evaluates how well the model detects negative cases, reducing false positives. Precision assesses the accuracy of positive predictions, especially important when false positives carry significant consequences. The F1 score balances precision and sensitivity, offering a combined metric that is particularly useful when dealing with imbalanced datasets. Together, these metrics provide a comprehensive view of a model's performance.

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN} \quad (10)$$

$$\text{Sensitivity} = \frac{TP}{TP+FN} \quad (11)$$

$$\text{Specificity} = \frac{TN}{TN + FP} \quad (12)$$

$$\text{Precision} = \frac{TP}{TP + FP} \quad (13)$$

$$\text{F1 score} = \frac{2\ X\ TP}{2\ X\ TP + FP + FN} \quad (14)$$

Where,

True Positives (TP): The number of correctly predicted positive samples.

True Negatives (TN): The number of correctly predicted negative samples.

False Positives (FP): The number of negative samples incorrectly predicted as positive.

False Negatives (FN): The number of positive samples incorrectly predicted as negative.

Performance of proposed AD-GNN model is compared with three existing work includes, work of Ghaffari, H., et. al., 2022, Klepl, D., et. al., 2022 and Fu'adah, Y.N., et. al., 2021

Ghaffari, H., et. al., 2022 used transfer learning with pre-trained CNN models for Alzheimer's disease classification from brain MRI. InceptionV3-TL achieved the highest accuracy and AUC, proving TL's superiority over training models from scratch. Klepl, D., et. al., 2022 compared eight functional connectivity (FC) measures for estimating brain graphs from EEG signals to classify Alzheimer's disease using GNN models. Fu'adah, Y.N., et. al., 2021 used a CNN based on the AlexNet architecture to classify Alzheimer's disease stages from MRI data, this automated classification

system aims to assist medical professionals in diagnosing Alzheimer's for timely treatment.

Table 2: Training and testing metrics of the proposed AD-GNN model

Epoch	Training Loss	Testing Loss	Training Accuracy	Testing Accuracy
10	0.201	0.24	0.963	0.96
20	0.165	0.218	0.972	0.968
30	0.247	0.202	0.953	0.951
40	0.252	0.262	0.959	0.956
50	0.241	0.198	0.954	0.95
60	0.213	0.175	0.952	0.951
70	0.135	0.22	0.961	0.958
80	0.194	0.281	0.973	0.964
90	0.198	0.185	0.96	0.958
100	0.168	0.209	0.964	0.957
Overall	**0.2014**	**0.219**	**0.9611**	**0.9573**

Table 2 provides overall performance metrics across 100 epochs, with an average training loss of 0.2014 and a testing loss of 0.219. The model achieved an average training accuracy of 96.11% and a testing accuracy of 95.73%, indicating strong generalization and consistent performance throughout the training process. These metrics suggest that the model maintains a good balance between learning the training data and generalizing to unseen data.

Table 3: comparative analysis among proposed AD-GNN and existing works of Ghaffari, H., et. al., 2022, Klepl, D., et. al., 2022 and Fu'adah, Y.N., et. al., 2021

Work	Sensitivity	Specificity	Accuracy	Precision	F1 Score
Proposed AD-GNN	0.93	0.94	0.96	0.93	0.92
Ghaffari, H., et. al., 2022	0.92	0.9	0.95	0.9	0.91
Klepl, D., et. al., 2022	0.97	0.98	0.92	0.93	0.92
Fu'adah, Y.N., et. al., 2021	0.9	0.9	0.94	0.91	0.9

Table 3 represents a comparison of performance metrics across different works in the domain of graph neural networks and related methodologies for image classification tasks. The Proposed AD-GNN achieves a sensitivity of 0.93, specificity of 0.94, accuracy of 0.96, precision of 0.93, and an F1 score of 0.92, indicating strong overall performance, particularly in its ability to correctly classify positive cases and overall precision. In comparison, Ghaffari, H., et. al., 2022 demonstrates slightly lower values, with a sensitivity of 0.92, specificity of 0.90, accuracy of 0.95, precision of 0.90, and an F1 score of 0.91. Klepl, D., et. al., 2022, while excelling in sensitivity 0.97 and specificity 0.98, has a lower accuracy of 0.92, with an F1 score of 0.92. Finally, Fu'adah, Y.N., et. al., 2021shows a balanced performance with a sensitivity and specificity of 0.90, an accuracy of 0.94, precision of 0.91, and an F1 score of 0.90. Overall, the Proposed AD-GNN outperforms previous works in accuracy while maintaining a competitive balance across other key metrics.

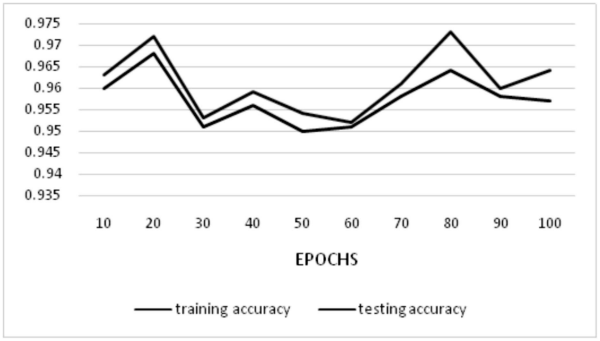


Figure 4: Shows the graphical presentation of training accuracy and testing accuracy of the proposed AD-GNN model

Figure 4 presents the graphical representation of both training and testing accuracy for the proposed AD-GNN model throughout the training period. The curves illustrate the model's performance, with the training accuracy demonstrating a consistent upward trend as the model learns from the data. In contrast, the testing accuracy reflects the model's ability to generalize to unseen data, providing a crucial assessment of its effectiveness. This figure highlights the overall success of the training process and the model's potential for accurate classification of Alzheimer's disease and cognitive impairment.

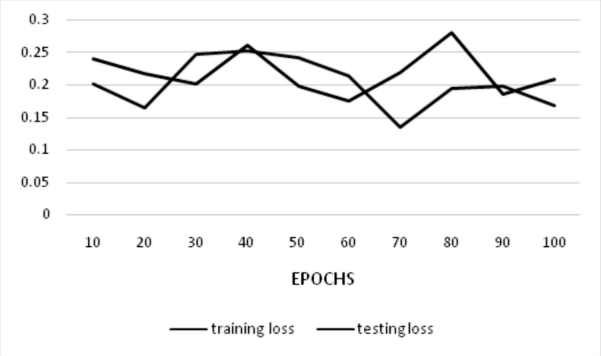


Figure 5: Demonstrates the graphical representation of the training loss and testing loss of the proposed AD-GNN model

Figure 5 illustrates the training and testing loss curves of the proposed AD-GNN model over the course of the training process. The graph clearly shows the progression of both losses, highlighting how the training loss decreases steadily while the testing loss reflects the model's performance on unseen data. This visualization provides insight into the model's learning dynamics and its ability to generalize, indicating the effectiveness of the training approach in minimizing loss and enhancing overall performance.

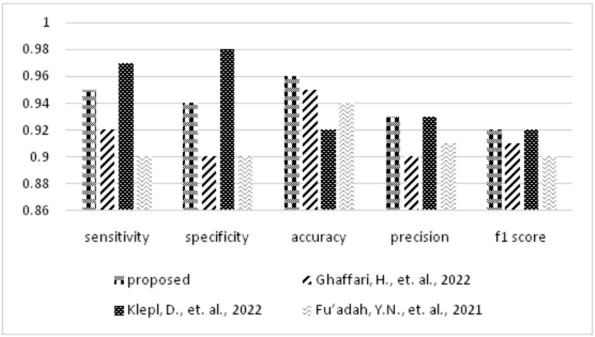


Figure 6: A graphical representation comparing the performance metrics achieved by the proposed work alongside those from Ghaffari, H., et. al., 2022, Klepl, D., et. al., 2022, and Fu'adah, Y.N., et. al., 2021.

Figure 6 presents a comparative graphical representation of the performance metrics achieved by the proposed work in relation to the studies conducted by Ghaffari, H., et. al., 2022, Klepl, D., et. al., 2022, and Fu'adah, Y.N., et. al., 2021. This visualization highlights the effectiveness of the proposed method, allowing for a clear assessment of its performance against existing approaches in the field. By showcasing key metrics, the figure illustrates the advancements made and emphasizes the contributions of the proposed work to the classification of cognitive impairment and Alzheimer's disease.

DISCUSSION

The proposed AD-GNN model demonstrates a significant performance advantage over existing methodos, including the works of Ghaffari, H., et. al., 2022, Klepl, D., et. al., 2022, and Fu'adah, Y.N., et. al., 2021. While these previous studies utilized conventional image classification techniques, often relying on pixel-wise analysis that may overlook complex spatial relationships within the brain, the AD-GNN leverages a graph-based approach to effectively capture the intricate connectivity patterns and structural features of MRI scans. By representing each pixel as a node in a graph and employing multiple graph convolutional layers, the AD-GNN not only enhances feature extraction but also improves the model's ability to generalize across varying brain structures. This leads to superior classification accuracy, allowing for a more nuanced differentiation between cognitive states, thereby addressing the limitations noted in earlier works and establishing a more robust framework for Alzheimer's disease detection.

V. CONCLUSION

This research presents an effective approach for classifying Alzheimer's disease and various stages of cognitive impairment using AD-GNN model. By transforming MRI brain images into graph structures, where pixels serve as nodes and edges capture local anatomical relationships, the AD-GNN effectively learned structural and spatial patterns in the brain. The model, composed of multiple graph convolutional layers and fully connected layers, was able to classify images into five categories: AD, CN, EMCI, LMCIand MCI. The use of global average pooling, combined with an optimized learning process,

facilitated efficient graph-level feature extraction and classification. The results demonstrate that the AD-GNN is capable of distinguishing cognitive states based on brain connectivity patterns, highlighting its potential for enhancing early diagnosis and intervention strategies in Alzheimer's disease. Future work could explore integrating additional modalities or expanding the model to larger datasets for improved generalization.

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