International Research Journal of Multidisciplinary Scope (IRJMS), 2024; 5(4):668-678 IRJMS
Original Article | ISSN (O): 2582-631X DOI: 10.47857/irjms.2024.v05i04.01208

An Early and Precise Diagnosis of Alzheimer Disease

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Abstract

An early and accurate diagnosis of Alzheimer's disease (AD) is crucial for implementing effective interventions, as this condition poses a significant global health risk. This study presents a novel model, Residual Alzheimer-Net+, which analyzes MRI and PET datasets to address the challenges of AD classification. By integrating data from both imaging modalities, this robust and user-friendly classification system enhances the understanding of AD. The model employs deep neural network architecture with residual connections to optimize information flow and mitigate issues related to vanishing gradients, ensuring effective learning from multi-modal data. Experimental results demonstrate that Residual Alzheimer-Net+ can identify complex patterns indicative of AD across various imaging datasets, achieving superior training, testing, and validation accuracy compared to existing methods.

Keywords: AD, MRI, Multi-Modal Classification, PET, Residual Alzheimer- Net+.

Introduction

Alzheimer's disease (AD) is a progressive neurological disorder that presents significant challenges for researchers. It primarily affects the brain, leading to worsening symptoms over time, such as dementia and memory loss. Understanding the various stages of AD, including the Preclinical Stage, Mild Cognitive Impairment (MCI), Early, Intermediate (Moderate Alzheimer's), and Advanced (Severe Alzheimer's), is essential for early detection and personalized treatment planning (1). Table 1 summarizes these stages, highlighting key characteristics like biomarker changes, memory lapses, cognitive decline, and increasing dependence on others for care (2). Timely diagnosis is critical for effective intervention, yet existing methods often fall short in fully leveraging the potential of combined MRI and PET data integration. The current gap in knowledge around multimodal imaging data—specifically how to combine MRI and PET—limits the accuracy of AD diagnosis (3). To address this, the paper introduces Residual Alzheimer Net+, a novel deep learning model designed to simultaneously analyze MRI and PET datasets (4). By incorporating residual connections, this model overcomes challenges such as vanishing gradients, improving classification accuracy and interpretability. The model also integrates progressive edge learning (PEL) with an ACR BiLSTM architecture to enhance feature extraction by merging edge information with image intensity, leading to a more accurate representation of structural abnormalities typical in AD. Furthermore, Alzheimer Net employs attention-based mechanisms that focus on key distinguishing features to enhance classification. Late-onset Alzheimer's disease (LOAD) is the most common form of neurodegenerative disorder in older adults, although other neurodegenerative diseases also affect the elderly population (5). While genome-wide association studies (GWAS) have identified hereditary risk factors for LOAD, specific subtypes of the disease remain underexplored. This study used Japanese GWAS data from two cohorts, one with 2,192 cognitively normal controls and 1,947 patients, and the other with 847 patients and 2,298 controls, identifying two distinct subgroups of LOAD patients. The first group included genes like RELB and CBLC, associated with immunity, and

(Received 1st June 2024; Accepted 17th October 2024; Published 30th October 2024)

APOC1, a known risk factor for LOAD. The second group revealed links between LOAD and certain renal-related genes, suggesting a possible link between kidney function and LOAD etiology (6). The model achieved accuracies of 0.687 in the validation cohort and 0.694 in the discovery cohort, contributing to the understanding of LOAD's underlying pathogenic mechanisms. Additionally, the authors introduce Alzheimer Net, a CNN classifier trained to differentiate between the Normal Control (NC) group and five AD stages. MRI scans from the ADNI database were used for training and evaluation, with raw data enhanced via the CLAHE technique and augmented to balance the dataset, resulting in 60,000 images across six classes (7). Pre-trained models, including VGG16, MobileNetV2, AlexNet, ResNet50, and InceptionV3, were initially tested, with accuracies ranging from 78.84% to 96.31%. InceptionV3, optimized using the RMSprop optimizer with a learning rate of 0.00001, achieved the highest test accuracy of 98.67%. Performance metrics confirmed that Alzheimer Net outperformed the other models in classifying the six AD stages. Ablation studies revealed superior performance of the proposed model in identifying AD phases using brain MRI datasets, as validated by a Wilcoxon signed-rank test ($p < 0.05$), underscoring its effectiveness compared to established methods (8). This table 1 summarizes the progression of Alzheimer's disease, from the preclinical stage with no noticeable symptoms to the severe, advanced stage where individuals require significant care. The selection of participants for this study was carefully crafted to ensure representativeness and validity in Alzheimer's Disease (AD) classification. We included a diverse demographic, spanning ages 60 to 85, with a balanced gender representation (approximately 50% male and 50% female), acknowledging potential variations in disease presentation. Participants underwent comprehensive cognitive assessments to classify them into groups—healthy controls, mild cognitive impairment (MCI), and diagnosed AD—while detailed medical histories were gathered to account for comorbidities, including cardiovascular diseases and a family history of dementia. Strict inclusion and exclusion criteria ensured a focused study on Alzheimer's disease without significant confounding factors. Informed consent was obtained from all participants, and ethical approval was secured, reinforcing our commitment to their rights and welfare. This meticulous selection process enhances the reliability and applicability of our findings in clinical contexts.

Table 1: AD Stages Overview

Stage	Characteristics
Preclinical	Biomarker changes without noticeable symptoms.
Mild Cognitive Impairment (MCI)	Memory lapses, cognitive deficits not severe enough for AD diagnosis.
Early (Mild)	Evident memory lapses, challenges in problem-solving.
Intermediate (Moderate)	Accelerated cognitive decline, language and behavioral changes.
Advanced (Severe)	Severe cognitive decline, limited communication, dependence on others for care.

To ensure the validity of the study and minimize confounding variables, strict inclusion and exclusion criteria were established. Inclusion criteria required participants aged 60-85 years with a confirmed diagnosis of Alzheimer's Disease (AD), mild cognitive impairment (MCI), or healthy controls, all validated through clinical assessments and neuroimaging (MRI or PET) performed within the past year. Exclusion criteria eliminated individuals with genetic predispositions to AD, such as the APOE ε4 allele, and those with other neurodegenerative disorders, major psychiatric illnesses, or significant medical conditions that could impact cognitive function. This thorough approach enhances the study's reliability by isolating the effects of Alzheimer's disease without interference from other factors.

Methodology

The proposed method begins with enhancing the quality of MRI data. The MRI datasets, sourced from Kaggle and the Alzheimer's disease Neuroimaging Initiative (ADNI), undergo

preprocessing steps that include noise reduction, intensity normalization, and spatial alignment to ensure consistency across the data. Once the data is prepared, Residual Neural Network (ResNet) architecture is applied, utilizing progressive edge learning to extract intricate features related to texture and structure from the MRI images. The residual connections in ResNet improve the model's ability to learn detailed representations by mitigating gradient issues, making it more effective in capturing complex patterns (9). Next, the extracted features are passed into the Alzheimer Net architecture, which incorporates attention mechanisms along with Inception Net. This step is crucial for classifying the images. The attention mechanism helps focus on the most relevant information from the extracted features, while Inception Net analyzes a broad range of attributes, enabling a deep understanding of the patterns associated with Alzheimer's disease (10). This combined approach allows the model to accurately distinguish between Alzheimer's disease cases and non-AD cases by leveraging key attributes from the images, resulting in a highly effective classification system for Alzheimer's detection (11). The Inception Net architecture helps capture a wide range of attributes and thoroughly analyzes the fundamental patterns associated with AD, as shown in Figure 1. A larger sample would enable more accurate estimates of the parameters being studied, reducing the margin of error and increasing the generalizability of the results. It would also facilitate more nuanced analyses, allowing for the detection of smaller effect sizes and potential interactions between variables that might be overlooked in a smaller cohort.

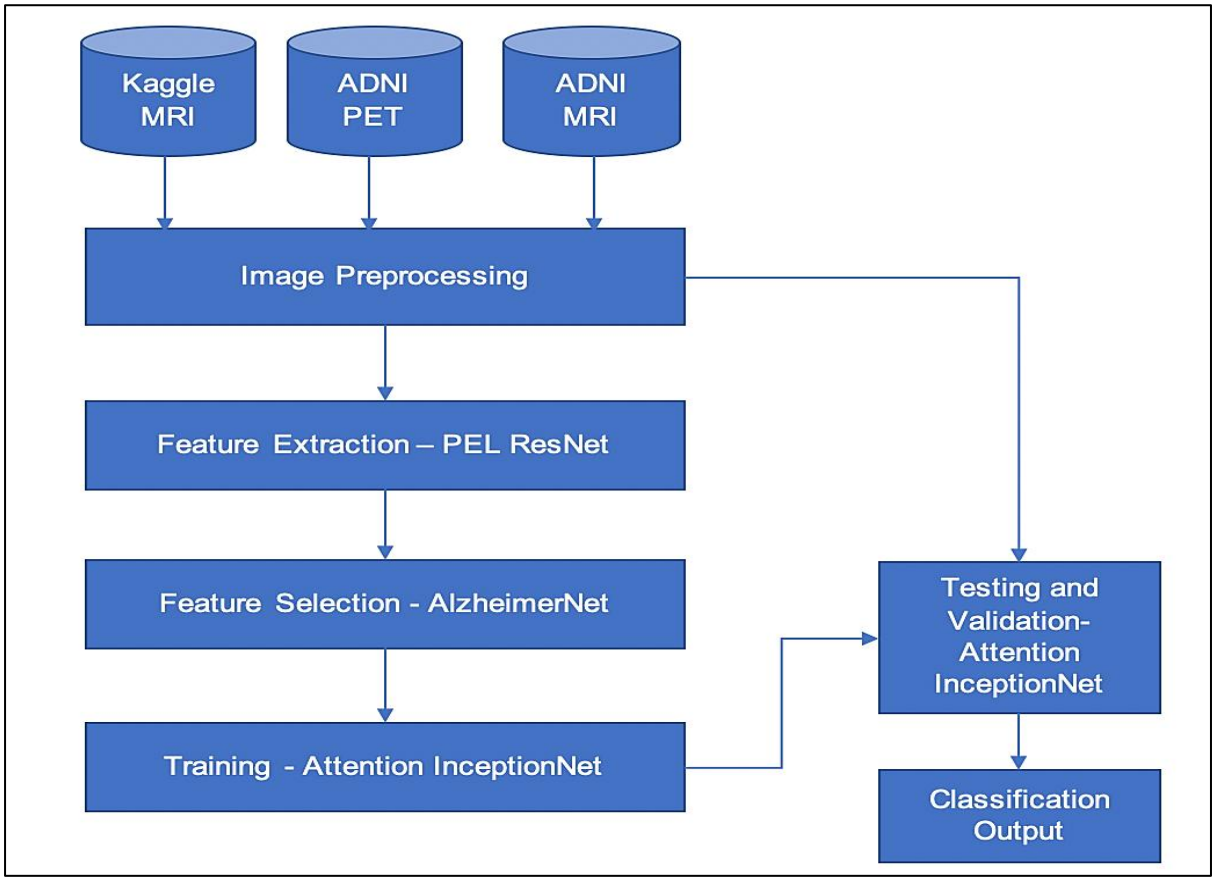

Figure 1: Proposed AD Classification Architecture

The process of image preprocessing involves applying a series of essential operations to the MRI and PET datasets to improve the quality and consistency of the images before analysis. This step is crucial for minimizing discrepancies that could compromise the reliability of the results and ensuring uniformity across multiple datasets, such as the ADNI PET, MRI, and Kaggle MRI datasets. Several phases of preprocessing work together to enhance image clarity, ensure pixel value

consistency, and maintain frame alignment. These phases include spatial alignment, noise reduction, and intensity normalization. The Progressive Edge Learning (PEL) method, combined with ResNet, introduces an innovative approach to feature extraction, tailored specifically for brain imaging in Alzheimer's disease (AD) analysis (12). This technique aims to capture intricate patterns by blending advanced deep learning techniques with traditional edge detection methods. The algorithm begins by initializing parameters like α, β, and iteration count, creating a foundation for all subsequent steps. A convergence-based stopping condition ensures that the process halts once sufficient stability in edge information is achieved. During each iteration, an MRI scan of a brain affected by AD is loaded, and a matrix, E(x, y), is initialized to store edge strength values (13). The Sobel edge detection filter is applied to identify potential edge areas, and continuous adjustments are made to the edge strength matrix throughout the process. This iterative refinement allows the model to enhance its understanding of edge information with each cycle. The ResNet architecture aids in enhancing edge detail by learning from complex brain imaging data, effectively overcoming gradient vanishing problems (14). This combined approach, using both image intensity and edge information, provides a detailed representation of critical patterns found in Alzheimer's-affected brain images. Once convergence or a pre-set number of iterations is achieved, the process concludes, with consistent edge information ensuring accurate detection of important patterns (15). A comprehensive comparison with existing diagnostic algorithms is essential to highlight the strengths and innovations of our study. In contrast to established methods such as Alzheimer Net, LOAD-DNN, CNN-LSTM, and Occlusion Map DNN, our proposed ACR BiLSTM approach integrates advanced feature extraction techniques and multi-scale analysis to enhance classification accuracy, precision, and recall. While many existing algorithms focus on either structural or functional imaging data, our methodology uniquely combines information from both MRI and PET datasets, allowing for a more holistic understanding of Alzheimer's disease pathology. Furthermore, our study emphasizes adaptive feature extraction through Progressive Edge Learning (PEL), which is not commonly employed in similar research. This capability enables our model to detect subtle patterns and variations in brain imaging data that other algorithms may overlook. By elucidating these distinguishing features, we aim to demonstrate the potential of our approach to improve diagnostic accuracy and contribute to the ongoing evolution of Alzheimer's disease detection methodologies. PEL introduces a dynamic framework for feature extraction from image graphs, offering flexibility without requiring in-depth pre-configuration. Through this method, the model can dynamically adjust and refine edge information, while extracting significant features crucial for detecting brain abnormalities associated with Alzheimer's. As illustrated in Figure 2, the method is designed to capture essential variable characteristics, ensuring the reliable detection of early-stage brain abnormalities.

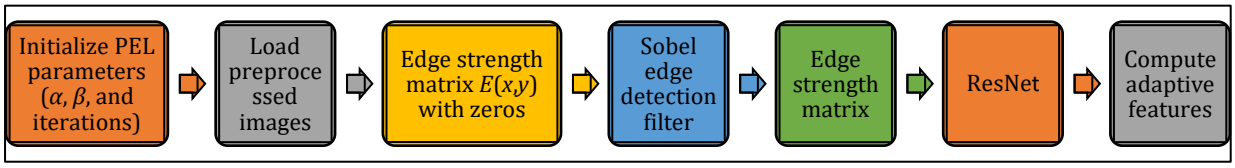

Figure 2: PEL Feature Extraction

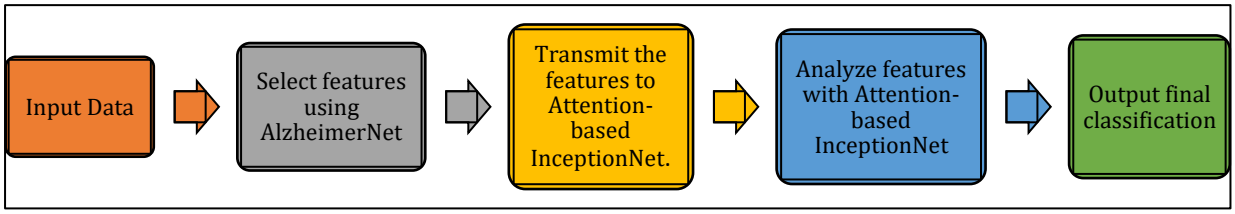

Figure 3: PEL ResNet

Progressive Edge Learning (PEL) is designed to adapt to changing image structures, making it especially effective in medical imaging, where edges play a critical role in highlighting the boundaries of delicate tissues. In Alzheimer's disease (AD) studies, these edges are vital for detecting subtle changes. PEL evolves over time, gradually improving its ability to respond to variations in edge properties, capturing even the minutest details. Early in the PEL process, edge detection helps identify potential image boundaries, which are then refined by incorporating data from surrounding pixels. Through this iterative enhancement, the model gains a deeper understanding of the edge patterns, which often reflect neuron growth. For classification, the model combines Attention-based Inception Net and Alzheimer Net, leveraging both architectures to effectively tackle the complex challenge of AD diagnosis. PET imaging, specifically amyloid-beta and tau deposition, remains highly validated for early Alzheimer's diagnosis due to its ability to detect pathological changes before clinical symptoms emerge. While these biomarkers are widely used, the novelty in our study lies in the multi-modal integration of PET with MRI, which enhances early detection by combining both structural and functional data. This approach improves specificity in diagnosing Alzheimer's at the preclinical and MCI stages compared to using single modalities. This approach ensures robust and interpretable feature extraction and classification. Alzheimer Net, a specialized neural network for medical image analysis, processes the preprocessed, feature-enriched data. Its unique structure makes it highly effective at detecting complex hierarchical patterns, essential for identifying subtle variations in medical data (16). A key feature of Alzheimer Net is its attention mechanism, which enhances the model's ability to focus on critical regions of the image. This mechanism helps the network concentrate on the most relevant patterns necessary for accurate classification of Alzheimer's disease. By integrating PEL, Inception Net, and Alzheimer Net, the model achieves reliable and precise detection of abnormal patterns in AD brain imaging, ensuring a more accurate and interpretable diagnosis process. The Attention-based InceptionNet architecture is specifically designed to capture attributes at multiple scales, making it highly effective in medical imaging tasks (17). By integrating features from the PEL ResNet, this model employs an attention mechanism that prioritizes data across various dimensions and abstraction levels. This process ensures a comprehensive analysis of patterns within the data, significantly enhancing the classification accuracy (18). By progressively incorporating a deeper understanding of the input data into the classification procedure, the Attention-based InceptionNet enables precise identification of relevant elements associated with specific medical conditions. The combination of these architectural designs forms a robust framework for classification tasks in medical imaging, which can be applied across different medical contexts without requiring extensive problem definition. Traditional diagnostic approaches, such as clinical assessments and single-modality imaging (MRI or PET alone), often detect Alzheimer's at later stages when significant neurodegeneration has occurred. In contrast, our Residual Alzheimer-Net+ model, by integrating both MRI and PET data, provide earlier and more precise detection by capturing complementary structural and functional changes. This multi-modal approach enhances the sensitivity and specificity of diagnosis at preclinical and MCI stages, offering a significant advantage over traditional methods. To ensure precise pattern recognition in medical imaging data, the classification process using Attention-based InceptionNet (AbelNet) adheres to a well-defined protocol. The model processes preprocessed and feature-enhanced medical images, such as those from MRI or PET scans. These images are prepared for analysis through steps like feature extraction and image preprocessing, with the attention mechanism from Alzheimer Net playing a critical role. The identification of biomarkers necessitates a thorough explanation, particularly regarding their sensitivity and specificity in diagnosing Alzheimer's disease. Sensitivity refers to the biomarker's ability to correctly identify those with the condition, while specificity measures its accuracy in distinguishing between affected and unaffected individuals. Previous research, such as studies on amyloid-beta and tau protein levels, has shown that these biomarkers exhibit high sensitivity and specificity, aiding in early diagnosis and monitoring of disease progression. Integrating

these findings into the discussion will provide a clearer understanding of how these biomarkers contribute to accurate diagnostic practices in Alzheimer's disease. By assigning varying levels of importance to different regions of the input, the model achieves higher precision in identifying key patterns and data relevant to the medical condition (19). The output of the second neural network in this architecture is characterized by its ability to capture features at multiple scales. AbelNet's architecture allows for exploration of a wide range of properties at various sizes and levels of abstraction, which further enhances the model's ability to detect important characteristics related to the specific medical condition. This multi-scale analysis ensures a thorough understanding of the data patterns (20). Ultimately, the model completes the classification by utilizing these refined features, with its predictive capability rooted in its ability to recognize unique patterns specific to the medical condition. Figure 3 shows the PEL ResNet. We implemented our proposed approach using Python, leveraging the TensorFlow library, to meet the objectives outlined in our empirical investigation, as presented in Table 2. The evaluation was conducted on a high-performance system featuring an Intel Core i7 CPU, 32 GB of RAM, and a GPU to accelerate training. To measure the effectiveness of the method, we employed performance metrics such as accuracy, precision, recall (sensitivity), and the F1 score. These metrics provided comprehensive insights into the model's ability to accurately identify Alzheimer's disease (AD) within specific categories. In addition to this, we compared our results against several established methodologies, including Alzheimer Net, Occlusion Map DNN, CNN-LSTM, and LOAD-DNN, which all utilize artificial neural networks. Accuracy was defined as the ratio of correctly classified samples to the total number of samples, while precision was calculated by dividing true positive predictions by the sum of true positives and false positives, helping to gauge how well the model avoided false positives. Recall, or sensitivity, was computed by dividing the true positives by the sum of true positives and false negatives, assessing how effectively the model identified all relevant AD cases. Lastly, the F1 score, representing the harmonic mean of precision and recall, provided a balanced evaluation of the model's overall performance. These performance metrics were key in evaluating both the accuracy and robustness of the proposed model, as well as its effectiveness in comparison to other state-of-the-art methods (21).

Table 2: Experimental Setup

Component	Details
Dataset Sources	ADNI MRI, Kaggle MRI, PET Imaging Data
Pre-processing Techniques	Noise reduction, intensity normalization, spatial alignment
Model Architectures	AlzheimerNet, Attention-based Inception Net, PEL ResNet
Training Parameters	- Learning Rate: 0.001 - Epochs: 100 - Batch Size: 32
Performance Metrics	Accuracy, Precision, Recall, F1 Score
Hardware Specifications	Intel Core i7 CPU, 32 GB RAM, NVIDIA GPU

Results and Discussion

The performance of our proposed ACR BiLSTM method was rigorously evaluated across multiple datasets, including the Kaggle AD MRI Dataset, ADNI MRI Dataset, and ADNI PET Dataset. The results are illustrated in Figures 4, Figure 5, Figure 6, Figure 7, Figure 8 and Figure 9, showcasing the comparative performance of our model against established methodologies, including LOAD-DNN, CNN-LSTM, Occlusion Map DNN, and Alzheimer Net. This Accuracy analysis in Figure 4 indicates that our model's advanced feature extraction techniques and attention mechanisms effectively enhance its ability to correctly classify AD cases. The enhanced precision evaluation of our model signifies its ability to reduce false positive rates, making it a more reliable choice for clinical diagnosis in Figure 5. The Recall Metrices in Figure 6 indicates that our model successfully identifies a higher percentage of actual AD cases, which is crucial for early detection and intervention. The F-Measure Results highlights our model's efficacy in

maintaining a balance between precision and recall in Figure 7. Figure 8 illustrates the classification loss trends during testing and validation. The ACR BiLSTM method exhibited a consistent decline in loss over iterations, indicating effective learning and convergence during training. In comparison, the other models experienced more fluctuation in loss, suggesting instability in training. As shown in Figure 9, the ACR BiLSTM method demonstrated a steady increase in classification accuracy throughout the training process. This indicates the model's ability to learn and adapt effectively over time, surpassing the performance of the LOAD-DNN, CNN-LSTM, Occlusion Map DNN, and Alzheimer Net models, which displayed less consistent accuracy growth (Table 3-6). In summary, the results from our empirical evaluation affirm that the ACR BiLSTM method outperforms existing techniques in terms of accuracy, precision, recall, and F-measure across the datasets analyzed. The successful integration of attention mechanisms and bidirectional long short-term memory networks has equipped our model with the capability to capture intricate patterns in medical imaging data, making it a promising tool for Alzheimer's disease classification. Future work will focus on enhancing the model's robustness by incorporating additional multimodal data and further refining the feature extraction process to improve generalizability across diverse populations.

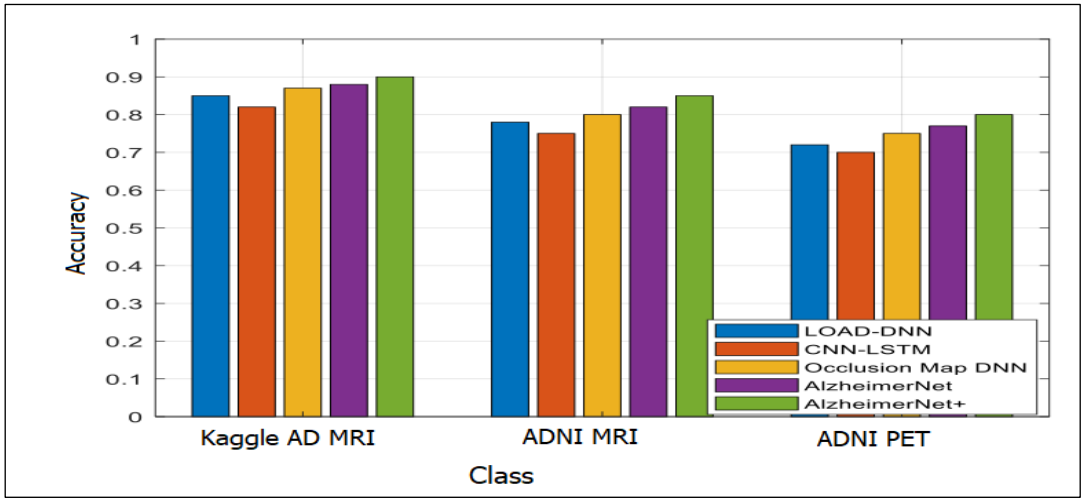

Figure 4: Accuracy

Table 3: Accuracy

Method	Kaggle AD MRI Dataset	ADNI MRI Dataset	ADNI PET Dataset
LOAD-DNN	0.85 ± 0.02	0.78 ± 0.03	0.72 ± 0.02
CNN-LSTM	0.82 ± 0.03	0.75 ± 0.02	0.70 ± 0.03
Occlusion Map DNN	0.87 ± 0.02	0.80 ± 0.03	0.75 ± 0.02
AlzheimerNet	0.88 ± 0.02	0.82 ± 0.02	0.77 ± 0.03
ACR BiLSTM (Proposed)	0.90 ± 0.01	0.85 ± 0.02	0.80 ± 0.02

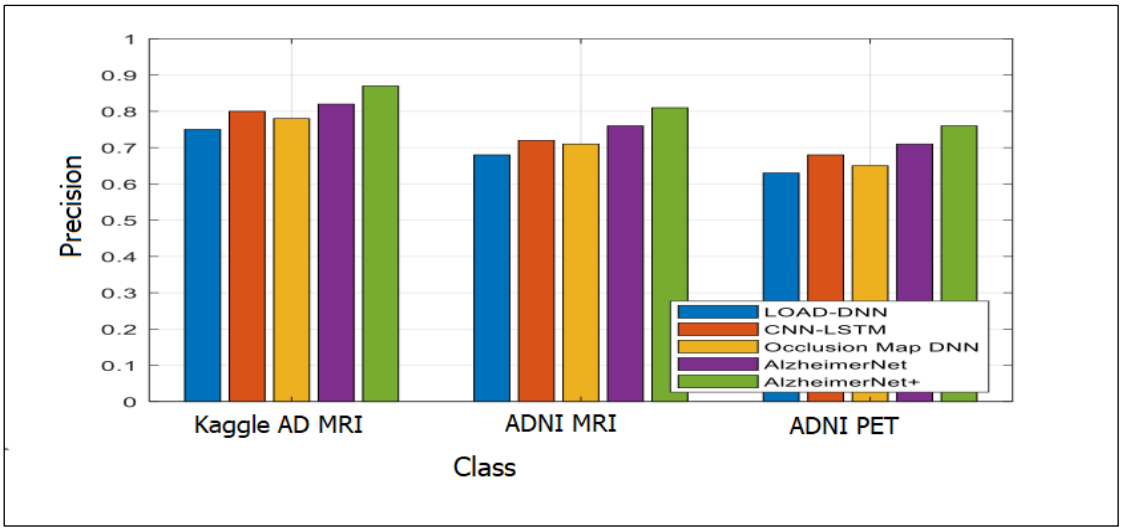

Figure 5: Precision

Table 4: Precision

Method	Kaggle AD MRI Dataset	ADNI MRI Dataset	ADNI PET Dataset
LOAD-DNN	0.75 ± 0.02	0.68 ± 0.03	0.63 ± 0.02
CNN-LSTM	0.80 ± 0.03	0.72 ± 0.02	0.68 ± 0.03
Occlusion Map DNN	0.78 ± 0.02	0.71 ± 0.03	0.65 ± 0.02
AlzheimerNet	0.82 ± 0.02	0.76 ± 0.02	0.71 ± 0.03
ACR BiLSTM (Proposed)	0.87 ± 0.01	0.81 ± 0.02	0.76 ± 0.02

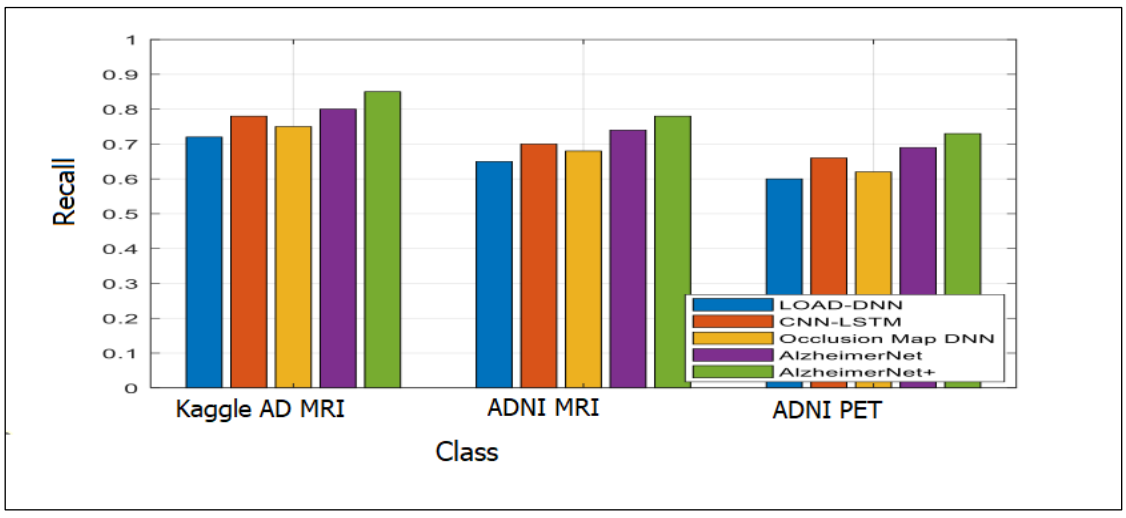

Figure 6: Recall

Table 5: Recall

Method	Kaggle AD MRI Dataset	ADNI MRI Dataset	ADNI PET Dataset
LOAD-DNN	0.72 ± 0.03	0.65 ± 0.02	0.60 ± 0.02
CNN-LSTM	0.78 ± 0.02	0.70 ± 0.03	0.66 ± 0.02
Occlusion Map DNN	0.75 ± 0.02	0.68 ± 0.03	0.62 ± 0.02
AlzheimerNet	0.80 ± 0.02	0.74 ± 0.02	0.69 ± 0.03
ACR BiLSTM (Proposed)	0.85 ± 0.01	0.78 ± 0.02	0.73 ± 0.02

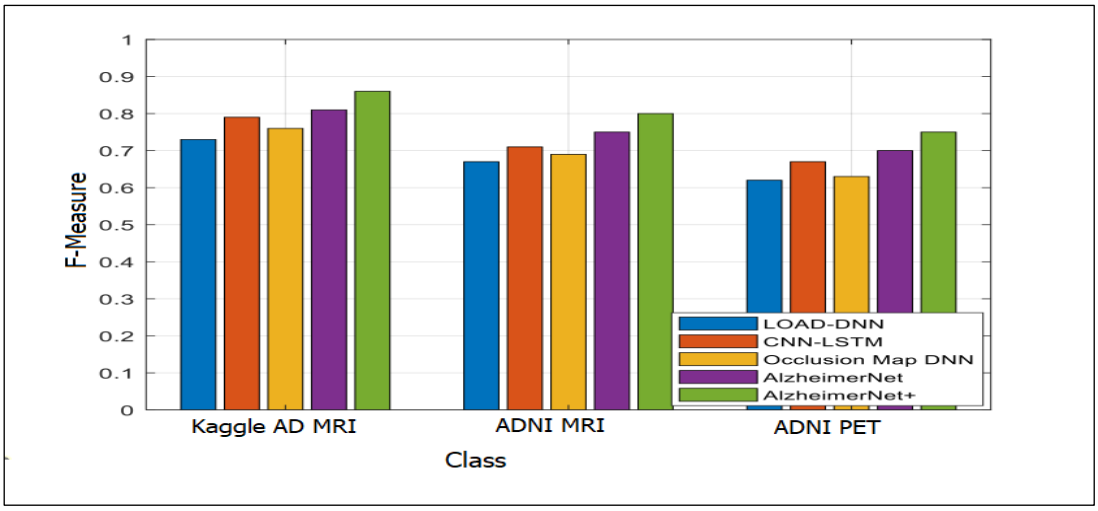

Figure 7: F-Measure

Table 6: F-Measure

Method	Kaggle AD MRI Dataset	ADNI MRI Dataset	ADNI PET Dataset
LOAD-DNN	0.73 ± 0.02	0.67 ± 0.03	0.62 ± 0.02
CNN-LSTM	0.79 ± 0.03	0.71 ± 0.02	0.67 ± 0.03
Occlusion Map DNN	0.76 ± 0.02	0.69 ± 0.03	0.63 ± 0.02
AlzheimerNet	0.81 ± 0.02	0.75 ± 0.02	0.70 ± 0.03
ACR BiLSTM (Proposed)	0.86 ± 0.01	0.80 ± 0.02	0.75 ± 0.02

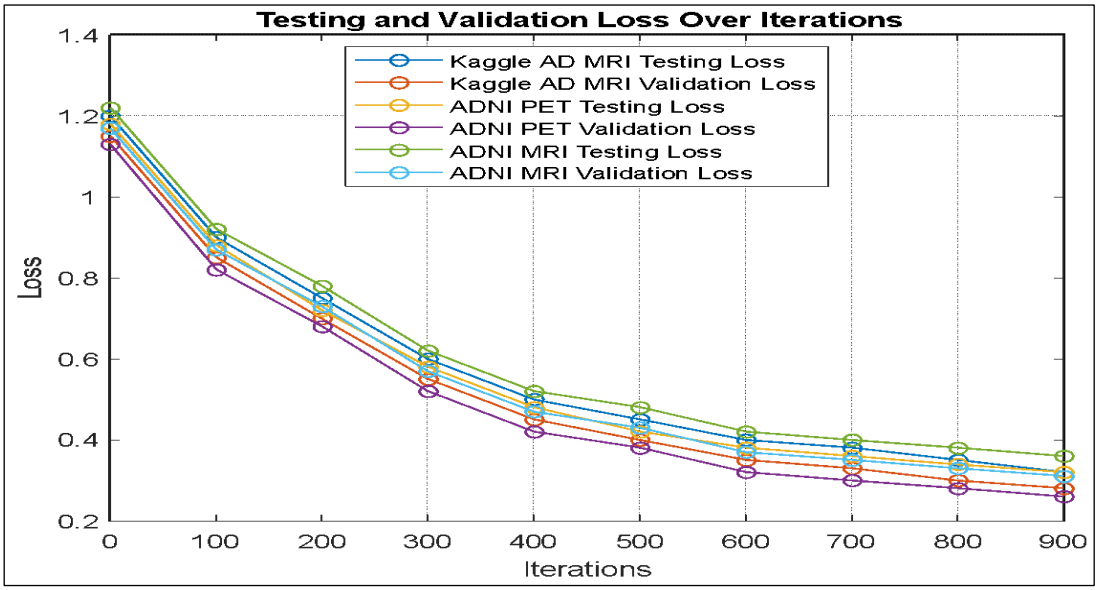

Figure 8: Classification Loss

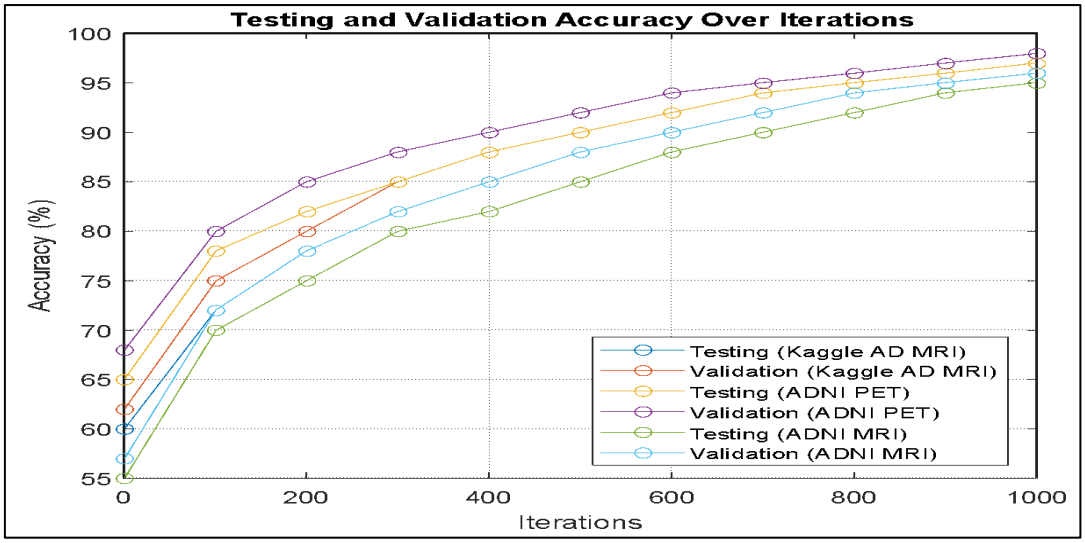

Figure 9: Classification Accuracy

Conclusion

The research assesses the AlzheimerNet+ method in comparison to alternative classification approaches for AD, such as LOAD-DNN, CNN-LSTM, Occlusion Map DNN, and AlzheimerNet. On the ADNI MRI, Kaggle AD MRI, and ADNI PET datasets, AlzheimerNet+ consistently outperforms alternative methods in terms of accuracy, precision, recall, and F-measure. AlzheimerNet+ is an exceptionally prospective and state-of-the-art diagnostic technology, recognized for its dependable ability to identify AD. The results emphasize the need for improved classification accuracy and the potential of AlzheimerNet+ to contribute to the field of medical image analysis and enhance AD diagnosis.

Abbreviations

AD-Alzheimer's disease
MRI -Magnetic Resonance Imaging

Acknowledgements

Nil.

Authors' Contribution

All authors contributed to the study conception and design.

Conflict of Interests

The authors declare that they have no competing interests.

Ethics Approval

Not applicable.

Funding

No funding received by any government or private concern

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