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Alzheimer’s Disease Detection

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1. INTRODUCTION

Abstract - Deep learning (DL) models are crucial for improving the early and accurate detection and classification of Alzheimer's Disease (AD) using Magnetic Resonance Imaging (MRI) scans, often focusing on biomarkers like hippocampal volume atrophy. Several novel DL architectures and methodologies have been introduced to enhance diagnostic precision: the ADD-Net, a novel Convolutional Neural Network (CNN) built from scratch, achieved 98.63% accuracy by classifying
AD stages and leveraging the hybrid SMOTETOMEK oversampling technique to address significant dataset imbalance; this model also utilizes GradCAM heat maps to highlight infected parts of the brain.

Similarly, another study utilizing an ensemble model of MobileNetV2 and DenseNet121 demonstrated that advanced image preprocessing using CLAHE (Contrast Limited Adaptive Histogram Equalization) and ESRGAN (Enhanced Super-Resolution Generative Adversarial Networks) significantly boosted MobileNetV2's accuracy to 92.34%, underscoring the efficacy of enhancement techniques. Furthermore, a fully automatic volumetric feature-based approach for AD versus Normal Control (NC) diagnosis aggregated a two-stage ensemble Hough-CNN for automatic hippocampal localization, a Discrete Volume Estimation CNN (DVE-CNN) to extract slice-wise volumetric features, and a Deep Neural Network (DNN) for final classification, achieving weighted accuracies of 94.82% (left hippocampus) and 94.02% (right hippocampus) on the GARD dataset. Despite these technological advancements, a mini - review notes that much of the existing research heavily relies on patients already known to have AD, which limits the knowledge gained regarding true initial detection.

Alzheimer’s Disease (AD) is a long-term, progressive neurological brain disorder marked by the gradual degeneration and decline of brain cells, leading to dementia, neurological dysfunction, memory loss, cognitive problems, and ultimately the loss of ability to perform dayto-day activities. It is the most frequent kind of dementia that requires substantial medical attention and is an incurable, fatal disease expected to affect 152 million patients by 2050. Since AD can begin developing a decade or more before clinical symptoms appear, the accurate diagnosis of AD in its early stages is extremely critical for ensuring patients receive timely intervention, preventive measures, and therapeutic treatment. While Magnetic Resonance Imaging (MRI), particularly Structural MRI (sMRI), is essential for diagnosis due to its capacity to identify key biomarkers like ADrelated brain atrophy and hippocampal volume atrophy, manual image evaluation is prone to observer variability. To overcome these limitations, Deep Learning (DL) and Artificial Intelligence (AI) methods have pioneered new, automated approaches to medical image diagnosis, offering systems that provide more consistent and accurate classification of brain MRI scans. Current research is advancing these methodologies through the development of specialized Convolutional Neural Network (CNN) architectures, like ADD-Net, which achieve high accuracy by reducing parameters; the use of advanced preprocessing techniques such as CLAHE and ESRGAN to enhance image clarity, which significantly improves the performance of classifiers like MobileNetV2; and the creation of fully automatic systems that utilize aggregated models to extract and classify slicewise volumetric features based on hippocampal volume reduction

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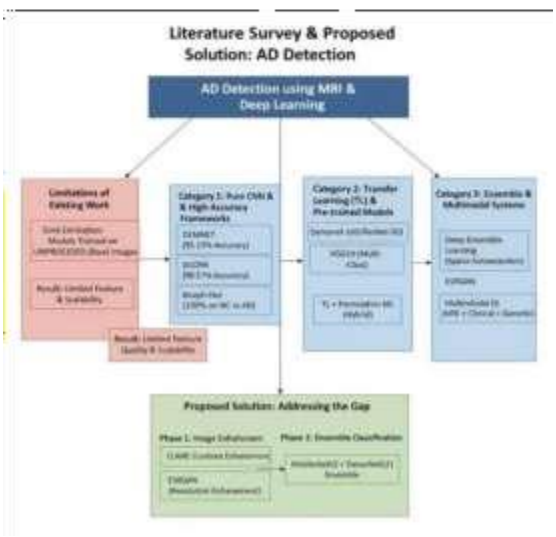
II .LITERATURE SURVEY



The following literature survey draws upon the analyses and related works sections presented across the sources, detailing the history, methodology, challenges, and current state of using deep learning algorithms for Alzheimer's Disease (AD) detection.

I. The Necessity of Automated AD Diagnosis and Biomarkers

Alzheimer's Disease (AD) is recognized as the most frequent kind of dementia, constituting a long-term, incurable, progressive neurological disorder characterized by the gradual destruction of brain cells, memory loss, and cognitive problems. Due to the enormous burden on the economy and families, and the projection that AD patients will reach 152 million by 2050, early detection is critical. AD can start developing a decade or more before clinical symptoms appear. Mild Cognitive Impairment (MCI) is often considered a pre-clinical, transitory state between normal aging and AD.

While AD diagnosis traditionally relies on manual evaluation of neuro-psychological examinations and patient MRI scans, this process is subjective and prone to variability among observers. Automated systems employing Deep Learning (DL) offer a more efficient approach to medical image diagnosis, capable of providing accurate results rapidly.

The automated systems primarily rely on established biomarkers. These measurable medical signs, such as beta amyloid ($\text{a}\beta 1-42$) plaque deposition, tau, and phosphorylated tau (ptau)181, are used to conclude the presence of a disorder. The most crucial and utilized biomarker in MRI-based DL research is Hippocampal Volume Atrophy (reduction), which leveraged for diagnosis include CT scans, PET scans, and SPECT scans.

II. Evolution From Machine Learning To Deep Learning

Early computational neuroscientific approaches applied traditional Machine Learning (ML) algorithms, such as Support Vector Machines (SVMs) and k-Nearest Neighbor (KNN), to classify patients by focusing on extracted features like regional cortical thickness or hippocampal volume measurements. These initial methods often required human intervention to define and retrieve handcrafted features, such as Gabor filters or Haralick texture features, from the images.

The limitations of traditional ML, especially concerning the manual effort involved and struggles with large datasets, led to the adoption of Deep Learning (DL). DL architectures, including
Convolutional Neural Networks (CNNs), Deep AutoEncoders (DAE), and Deep Belief Networks (DBN), aim to automatically discover unknown hidden representations and extract distilled features from input data.

III. Current Deep Learning Methodologies and Performance

Recent research focuses on enhancing accuracy and efficiency using refined DL models: Novel Architectures and Feature Focus:
- Many researchers have relied on Transfer Learning (TL), fine-tuning pre-trained architectures (like VGG19, DenseNet169, InceptionResNet V2, and MobileNetV2) to address problems like gradient vanishing and parameter reduction.
- Custom models have been developed, such as **ADD**Net, a CNN built from scratch specifically to reduce parameters and calculation costs for classifying AD stages.
- Other advanced frameworks include DEMNET (Deep CNN achieving 95.23% accuracy), a hybrid framework using ResNet V2 with Inception V4, and ensemble patch-based classifiers.
- A significant trend involves aggregating specialized models, such as the automatic system combining a two-stage ensemble Hough-CNN for localization, a
Discrete Volume Estimation CNN (DVE-CNN) for extracting slice-wise volumetric features, and a Deep Neural Network (DNN) for final AD vs. NC classification.

2. Performance Benchmarks: Models have shown high classification accuracy, particularly when data challenges are mitigated.
- ADD-Net achieved an accuracy of 98.63% on the balanced Kaggle dataset.
serves as an early diagnostic indicator visible in Structural MRI (sMRI). Other imaging techniques

IV. CHALLENGES AND MITIGATION TECHNIQUES

DL applications in medical imaging face inherent hurdles, primarily related to data quality and availability.
Dataset Imbalance: Medical datasets like the Kaggle MRI dataset (6400 samples) and OASIS are often highly

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imbalanced, making it challenging to compile equal numbers of health and ailment samples.

1.1 This issue can be addressed through **cost**sensitive training, or, more effectively, through synthetic oversampling.

1.2 The hybrid algorithm SMOTETOMEK is specifically employed to resolve this problem by generating new instances through interpolation, thereby balancing the class distribution and significantly boosting the AUC and accuracy of classification models.

2.Image Quality and Resolution: MRI images often exhibit low contrast and resolution, which can impede accurate feature extraction.

2.1 Image Enhancement Techniques are used to improve quality. These include CLAHE (ContrastLimited Adaptive Histogram Equalization) to optimize local contrast and visibility of refined features, and ESRGAN (Enhanced Super- Resolution Generative Adversarial Networks) to improve image resolution and accuracy. The utilization of these preprocessing techniques demonstrated a significant enhancement in performance, particularly for lightweight models like MobileNetV2, emphasizing the importance of image quality.

3.Model Interpretation (Black-Box Nature): Due to the "black-box nature" of CNNs, researchers utilize visualization techniques to understand the classification process. **Grad-CAM (Gradientweighted Class Activation Map)** is employed to generate heat maps that highlight the **discriminative regions** or "infected part" of the brain that substantially affect the deep model's prediction, providing critical insight into layer functionality and severity

V. Gaps and Future Directions A key limitation across the literature is that much of the existing work focuses on patients already known to have AD or MCI, thereby contributing less knowledge to true initial, pre-clinical detection. Furthermore, a philosophical difference separates current models: while many use Transfer Learning, resulting in models with numerous parameters, the proposed ADD-Net attempts to address this by building a customized CNN from scratch to decrease parameters and calculation costs.

I. Evolution of Diagnostic Techniques

- A DCNN model by Kundaram and Pathak achieved 98.57% accuracy in classifying AD, MCI, and Normal Control.

The need for automated diagnosis stems from the fact that manual evaluation of patient MRI scans and neuro-psychological examinations is often subjective and requires expert specialists.

A. Transition from Machine Learning (ML) to Deep Learning (DL):

- **Traditional ML:** Early approaches used traditional ML methods, such as Support Vector Machines (SVM) and kNearest Neighbors (KNN), typically utilizing handcrafted features (e.g., Gabor filters, Haralick texture features). These required manually defined feature descriptions, often neglecting strong texture descriptors.
- **Shift to DL: Deep Learning (DL)**, particularly Convolutional Neural Networks (CNNs), emerged to overcome the limitations of ML by automatically discovering unknown hidden representations and extracting distilled features from input data. DL architectures include generative models (Recurrent Neural Networks (RNN), Deep Auto-Encoders (DAE), Deep Boltzmann Machines (DBM), Deep Belief Networks (DBN)) and discriminative models (CNN and RNN). CNNs are preferred for their effectiveness in image-based problemsolving and their translation-invariant nature.

II. Deep Learning Architectures and Feature Focus

Researchers have leveraged and customized various DL models for AD detection:

- **Transfer Learning (TL):** Many studies rely on TL, fine-tuning pre-trained architectures like VGG19, DenseNet169, ResNet, InceptionResNet V2, and MobileNetV2, to enhance performance and reduce computational costs, especially with smaller datasets.
- **Custom/Novel CNNs:** Novel architectures designed from scratch, such as the proposed ADD- Net, aim to reduce parameters and calculation costs while achieving high accuracy, making them ideal for smaller datasets. Other custom CNN models mentioned include DEMentia NETwork (DEMNET), achieving 95.23% accuracy, and 12- layer CNN architectures using Leaky ReLU to avoid gradient vanishing issues, achieving up to 97.75% accuracy on the OASIS dataset.

Ensemble and Hybrid Frameworks: Combining models, such as using ResNet V2 with Inception V4, with ML classifiers (Naïve Bayes, SVM, and XGBoost) through a voting process, achieving 91.75% accuracy.

II.DATA CHALLENGES AND MITIGATION STRATEGIES

A significant body of work focuses on solving inherent limitations in medical image datasets: **1.Data Imbalance:** Medical datasets are highly imbalanced, meaning it is difficult to compile an equal number of health and ailment samples. The Kaggle MRI dataset, for example, is highly imbalanced with 6,400 samples distributed unevenly across four classes (NOD, VMD, MD, MOD).

1.1 Mitigation: Techniques used include costsensitive training (adjusting loss for minority classes), and generating synthetic samples via oversampling.

1.2 The SMOTETOMEK hybrid algorithm (combining SMOTE oversampling and TOMEK down-sampling) is specifically noted for interpolating new samples and successfully balancing the AD dataset.

2.Image Quality: MRI images often suffer from low contrast and resolution, demanding precise feature extraction.

2.1 Mitigation: Image Enhancement techniques like CLAHE (Contrast Limited Adaptive Histogram Equalization) enhance local contrast and visibility, and ESRGAN

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(Enhanced Super- Resolution Generative Adversarial Networks**)** improve resolution and accuracy. These preprocessing methods are crucial for optimizing input images, especially for lightweight models like MobileNetV2.

3.Model Interpretation (The "Black-Box" Problem): Due to the complexity of deep models, interpretation is challenging.

3.1 Mitigation: The Grad-CAM (Gradient- weighted Class Activation Map) algorithm is used for visualization, generating heat maps that highlight the discriminative regions or "infected parts" of the brain that influence the model's prediction, thereby offering insight into layer functionality and disease severity.

IV. NEUROIMAGING DATASETS

Researchers rely on specific medical data repositories that often require screening processes due to the sensitive nature of patient information:

- **ADNI(Alzheimer'sDiseaseNeuroimaging Initiative):** A widely used repository that provides T1-weighted structural MRIs, PET, and biological markers to study the progression of MCI and early AD. It includes 3D image formats and is known for its gigantic size (450 GB).

  or ensembles of patch-based classifiers, has been explored to improve diagnostic capabilities. A hybrid AI model integrated TL models (DenseNet- 121 and
- **OASIS (Open Access Series of Imaging Studies):** Provides 3D samples for young, middle-aged, nondemented, and demented older adults (416 cases mentioned in one study).
- **Kaggle MRI Image Dataset:** A multi-class dataset of 6400 samples used for classification into NOD, VMD, MD, and MOD, selected due to its manageable size and organized, pre-cleaned nature.
- **GARD (Gwangju Alzheimer's and Related Dementia) Dataset:** A private dataset consisting of 326 MRI scans used for AD vs. NC classification, specifically focusing on Korean subjects.

V. Limitations Identified in Existing Literature Despite significant progress in accuracy, a critical limitation persists across the field:

- **Lack of True Initial Detection:** Most published studies focus on patients already known to have AD or MCI (Mild Cognitive Impairment), which limits the knowledge generated regarding true initial or preclinical detection before the disease manifests itself.
- **Model Efficiency:** Many models relying on transfer learning, while accurate, contain a large number of parameters, potentially affecting network efficiency.
- **Feature Selection and Loss:** Not all features extracted by deep models are useful, and some can hinder results. Researchers have proposed methods using optimization algorithms (Rival Genetic Algorithm (RGA) and Probability Binary Particle Swarm Optimization (PBPSO)) for selective feature extraction to improve classification and reduce training time.

III. LIMITATION OF EXISTING SYSTEMS

Based on the sources, the limitations of existing systems and methodologies for Alzheimer's Disease (AD) detection using deep learning can be categorized into issues related to data, models, methodology, and scope.

I. Data and Preprocessing Limitations A major constraint frequently encountered in the existing literature concerns the availability and characteristics of medical datasets:

- **Data Imbalance:** Medical datasets are inherently highly imbalanced because it is challenging to compile a data set with an equal number of patients having health and (NOD, VMD, MD, MOD). The minority classes (VMD, MD, MOD) have significantly fewer images compared to the majority class (NOD).
- **Model Compromise due to Imbalance:** The efficiency of deep learning models, including the proposed **ADD-Net**, suffers on the imbalanced dataset . The accuracy of previous methods was compromised on AD datasets due to the unequal number of classes.
- **Data Size and Accessibility:** Large public datasets like ADNI(450 gigabytes) and OASIS (18 gigabytes) are often in 3Dimensional image format and are gigantic in size, making them difficult to handle. Furthermore, accessing these datasets requires a screening process (application and agreement to terms) because they contain sensitive and private patient information.
- **Raw Image Quality:** The majority of existing experiments have focused on training DL models using unprocessed images, which restricts the potential for the classification network to be scaled up. MRI images often exhibit low contrast and resolution, which can impede accurate discernment and categorization of AD.

II.Model and Architecture Limitations Limitations are also noted regarding the deep learning architectures commonly used prior to the proposed improvements:

- **Reliance on Transfer Learning (TL):** Many previous models utilized transfer learning, meaning they contained many parameters, which negatively affects the network's efficiency.
- **Black-Box Nature:** The focus of previous deep models is primarily biased towards classification due to the black-box nature of CNNs, making interpretation challenging.
- **Feature Loss in Specific Architectures:** When using DenseNet121, the primary drawback is the potential loss of critical features caused by the bottleneck approach employed in DenseBlocks, which might lead to poor convergence and overfitting.
- **Computational Constraints**: When the depth and width of the network design expand, DenseNet121 may require a significant amount of processing resources. Conversely,

MobileNetV2, while efficient and lightweight, may occasionally limit its ability to perform deep feature extraction due to its focus on efficiency and speed.

initial successes of custom models like ADD-Net. ailment samples. For instance, the Kaggle MRI image dataset has a significant class imbalance problem across its four classes

III.METHODOLOGICAL AND SCOPE LIMITATIONS

A critical limitation concerns the real-world utility and methodological reliance of the developed systems:

Limited Insight into True Initial Detection: Most machine detection methods are limited by congenital observations. The majority of selected patients in published papers are already known to have AD or have a forerunner of AD, such as Mild Cognitive Impairment (MCI). This adds little knowledge to the initial detection of AD, as prediction is only applicable before the disease manifests itself.

- **Dependence on Sub-Model Accuracy (Aggregated Systems):** For aggregated systems, such as the volumetric featurebased approach, the proposed method highly depends on the accuracy of the previously utilized automatic localization (HoughCNN) and discrete volume estimation (DVE- CNN) methods. If these upstream methods fail, the entire classification performance is problematic.
- **Manual Steps (Previous Work):** Some prior methods required manual localization, which is a complicated and time-consuming task.

IV. FUTURE SCOPE

Based on the analysis of the sources provided, the future scope for research in the automated detection and classification of Alzheimer's Disease (AD) using deep learning focuses primarily on enhancing model accuracy, improving robustness and efficiency, and expanding the scope beyond single-modality data. The future goals for this research area include the following objectives:

- Enhancing Model Performance and Efficiency Mitigating Model Limitations: Future work is proposed to use sophisticated hyper- parameter optimization strategies to tackle the existing limitations of specific models, such particularly MobileNetV2.
- Addressing Feature Loss: Researchers aim to investigate hybrid architectures that merge DenseNet with other models to alleviate potential feature loss, a primary drawback caused by the bottleneck approach in DenseBlocks of DenseNet121, and to minimize overfitting.
- Involving Transfer Learning: There is a plan to involve other pre-trained architectures and fine-tune transfer learning models to achieve
- **Improving Generalization:** The model's generalization capabilities on varied datasets might be further improved by implementing more advanced data augmentation procedures.

II. Expanding Data Modality and Integration

The field intends to move beyond relying solely on structural MRI data to enhance diagnostic robustness:

- **Multi-Modality Integration:** Subsequent research should prioritize the improvement of DL models by integrating many types of data, such as merging MRI with other imaging techniques or including genetic and clinical data to achieve better diagnostic accuracy.
- **Open Dataset Validation:** Specifically concerning the volumetric feature-based diagnosis, future plans include applying the method to large open source datasets and combining the volumetric features of the left and right hippocampi with data of other modalities, such as Positron Emission Tomography (PET).
- **Feature Combination:** Future research will explore combining volumetric features with other regional features, such as VBM (Voxel-Based Morphometry) and CSC (Cortical and Subcortical volumetric features.

III.Clinical Application and Preprocessing Refinement

- **Advanced Preprocessing:** The advancement of the discipline could be furthered by the development of **more intricate preprocessing** algorithms that are customized to meet specific diagnostic requirements.
- **Real-World Implementation:** There is a goal to investigate the implementation of these improved models in real-world clinical environments.
- **Impact on Timely Detection:** By further integrating technical breakthroughs with clinical needs, future research can significantly impact the timely and precise detection of Alzheimer's Disease, thereby enhancing patient outcomes.

V. CONCLUSION

The conclusion of the paper, "ADD-Net: An Effective Deep Learning Model for Early Detection of Alzheimer Disease in MRI Scans," summarizes the achievements of the proposed architecture and outlines future work.

The research proposed a novel deep Convolutional Neural Network (CNN) for detecting Alzheimer's more desirable classification results, building upon the Disease (AD) , which is designed with relatively few parameters, making it ideal for training a smaller dataset.

This model, named the Alzheimer's Disease Detection Network (ADD-Net), was built from scratch to precisely classify the stages of AD by decreasing parameters and calculation costs ..Each block within the network is specifically termed an ADD-block, utilized to classify AD in its early stages for all specific classes , . To address the central problem of the imbalanced data-set, the SMOTETOMEK method was employed for generating new instances to balance the number of samples for each category , , . Furthermore, the GradCAM algorithm provides insight into the CNN layers' workings by visualizing class activation heat-maps , . The proposed deep model achieved outstanding accuracy of 96.70%, 97% precision, Sensitivity (Recall) of 97%, and an impressive AUC value of 99.82% , , . Looking forward, the authors stated plans to involve other pre-trained architectures and finetune transfer learning models to achieve more desirable classification results in future research , .

VI. REFERENCES

The four IEEE papers analyzed for Alzheimer's Disease (AD) detection using deep learning are detailed below:

1. ADD-Net: An Effective Deep Learning Model for Early Detection of Alzheimer Disease in MRI Scans

- **Title:** "ADD-Net: An Effective Deep Learning Model for Early Detection of Alzheimer Disease in MRI Scans".
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