

ConvADD: Exploring a Novel CNN Architecture for Alzheimer's Disease Detection

Mohammed G Alsubaie¹, Suhuai Luo², Kamran Shaukat³

School of Information and Physical Sciences, The University of Newcastle, Callaghan, NSW 2308, Australia^{1,2,3}
Department of Computer Science, College of Khurma University College, Taif University, Taif, 21944, Saudi Arabia¹

Abstract—Alzheimer's disease (AD) poses a significant healthcare challenge, with an escalating prevalence and a forecasted surge in affected individuals. The urgency for precise diagnostic tools to enable early interventions and improved patient care is evident. Despite advancements, existing detection frameworks exhibit limitations in accurately identifying AD, especially in its early stages. Model optimisation and accuracy are other issues. This paper aims to address this critical research gap by introducing ConvADD, an advanced Convolutional Neural Network architecture tailored for AD detection. By meticulously designing ConvADD, this study endeavours to surpass the limitations of current methodologies and enhance accuracy metrics, optimisation, and reliability of AD diagnosis. The dataset was collected from Kaggle and consists of preprocessed 2D images extracted from 3D images. Through rigorous experimentation, ConvADD demonstrates remarkable performance metrics, showcasing its potential as a robust and effective. The proposed model shows remarkable results with a tool for AD detection accuracy of 98.01%, precision of 98%, recall of 98%, and an F1-Score of 98%, with only 2.1 million parameters. However, despite its promising results, several challenges and limitations remain, such as generalizability across diverse populations and the need for further validation studies. By elucidating these gaps and challenges, this paper contributes to the ongoing discourse on improving AD detection methodologies and lays the groundwork for future research endeavours in this domain.

Keywords—Alzheimer's disease; AD detection; convolution neural network

I. INTRODUCTION

Alzheimer's disease (AD) poses an escalating challenge in healthcare, demanding sophisticated and timely diagnostic mechanisms to enable prompt interventions and elevate the quality of patient care [1]. The persistent rise in dementia incidence, currently at a staggering 10 million new cases annually [2], signals an impending crisis, with forecasts indicating that the population afflicted by AD will soar to 152 million by 2050 [2]. This exponential growth trajectory not only underscores the pressing demand for precise diagnostic approaches but also emphasises the critical necessity for inventive and resilient detection frameworks to alleviate the impending healthcare burden.

The pathological mechanisms driving Alzheimer's disease (AD) unveil a tumultuous cascade of neuronal degeneration,

precipitating a profound decline in cognitive functions and the gradual erosion of memory capabilities [3]. This devastating progression is propelled by the insidious accumulation of proteins within the neuronal environment, instigating consequential structural alterations in the intricate architecture of the brain [4], [5], [6], [7]. Despite this disease's profound impact and relentless advancement, the quest for a precise diagnostic methodology remains an elusive endeavour, impeding the development of effective therapeutic interventions [8], [9], [10]. The imperative for early detection of Alzheimer's disease assumes paramount significance, particularly in identifying its nascent stage, Mild Cognitive Impairment (MCI). This preclinical phase signifies a pivotal juncture, spotlighting the crucial window for intervention and strategic treatment planning. Recognising MCI enables proactive measures aimed at mitigating disease progression, potentially forestalling the onset of debilitating symptoms and enhancing patient outcomes. Consequently, the development of robust diagnostic modalities capable of discerning subtle cognitive changes at this incipient stage holds profound implications for advancing both clinical management and therapeutic innovation in Alzheimer's disease [11], [12].

The landscape of Alzheimer's disease (AD) detection has undergone a transformative evolution catalysed by breakthroughs in neuroimaging methodologies and the emergence of computer-aided diagnostic approaches [7]. These pioneering innovations have revolutionised the field, furnishing clinicians with unprecedented insights into the intricate neuronal manifestations inherent to AD. Yet, notwithstanding the commendable strides achieved through machine learning [13] and deep learning [14] models, significant limitations persist in the realm of AD detection.

Machine learning algorithms have shown promise in identifying patterns indicative of Alzheimer's disease (AD) pathology from neuroimaging data. However, challenges persist in achieving consistent accuracy rates across diverse patient groups and imaging methods due to data variability, limited sample sizes, and the heterogeneous nature of AD. Interpretability remains a concern, as black-box models lack

transparency in explaining diagnostic predictions. Deep learning techniques offer the potential to extract features from neuroimaging data but require large, labelled datasets for effective training and are prone to overfitting. Integrating these algorithms into clinical practice necessitates rigorous validation and standardisation protocols alongside ethical considerations regarding patient privacy, data security, and algorithmic bias.

In light of these challenges, concerted efforts are underway to address the existing gaps in AD detection through interdisciplinary collaborations, data harmonisation initiatives, and the development of interpretable machine learning frameworks. By surmounting these obstacles, the field stands poised to realise the full potential of artificial intelligence in revolutionising early detection and personalised management strategies for Alzheimer's disease.

Remarkable advances in machine learning and deep learning models have indeed propelled the field of Alzheimer's disease detection forward, primarily through classification paradigms [15], [16], [17], [18]. These models have exhibited commendable abilities to discern intricate patterns and categorise data, offering promising avenues for early diagnosis and intervention. However, the predominant emphasis on classification may inadvertently overlook the nuanced complexities inherent in Alzheimer's disease pathology.

Alzheimer's disease involves complex neurodegenerative processes, including cognitive decline and various brain alterations. Early disruptions in synaptic function and signalling precede clinical symptoms by years. Amyloid-beta plaques and tau protein tangles lead to widespread neuronal dysfunction and cognitive decline. Machine learning and deep learning models excel in classification tasks but may oversimplify Alzheimer's complex pathology. A holistic approach is needed to capture disease progression and clinical diversity accurately.

To address this challenge, there is a growing recognition of the importance of integrating multimodal data sources and leveraging advanced analytical techniques that can capture the multidimensional nature of Alzheimer's disease. By combining neuroimaging data with clinical, genetic, and molecular biomarkers, researchers aim to construct comprehensive disease signatures that capture the diverse manifestations of Alzheimer's pathology across different stages of disease progression and patient subpopulations.

The use of classification-focused deep learning models has posed significant challenges in effectively capturing the spectrum of multifaceted manifestations of Alzheimer's disease. While these models excel at categorising data into discrete classes, they often fall short in capturing the complex

interplay of subtle neuronal abnormalities that characterise the onset and progression of AD. By primarily focusing on distinguishing between healthy and diseased states, these models may overlook the heterogeneity of AD pathology and fail to capture the nuanced changes occurring within the brain over time.

There is, therefore, a compelling imperative to transcend the limitations of classification-based models and embrace a paradigm that comprehensively encompasses the multiple facets of Alzheimer's disease pathology. Rather than simply categorising data into binary outcomes, it is essential to adopt a new approach that not only identifies patterns but also discerns the subtle and intricate nuances indicative of the early stages of Alzheimer's disease. This shift towards a more nuanced and comprehensive diagnostic framework holds the potential to enhance our understanding of AD pathogenesis and improve the accuracy of early detection strategies.

Our research introduces ConvADD, a novel convolutional neural network (CNN) architecture specifically tailored for accurate Alzheimer's disease detection. Unlike traditional models, ConvADD effectively handles imbalanced datasets without requiring extensive data augmentation. It features adapted convolutional blocks and deep layers optimised for discerning subtle disease patterns, even with smaller datasets. ConvADD represents a paradigm shift in Alzheimer's disease detection, overcoming dataset imbalances and revolutionising diagnosis. Leveraging advanced deep learning techniques, it offers promising potential for early detection and improved management, advancing our pursuit of effective treatments.

The contributions outlined highlight significant advancements in the field of Alzheimer's disease (AD) detection, particularly focusing on the development of ConvADD, a novel Convolutional Neural Network (CNN) architecture tailored specifically for this purpose. Here's an elaboration:

- The first major contribution is the creation of ConvADD, which stands for Convolutional Alzheimer's Disease Detection. This architecture represents a pioneering approach designed explicitly for detecting Alzheimer's Disease. Unlike previous models, ConvADD is crafted to prioritise accuracy without relying on dataset-balancing techniques. This means that it can maintain robust performance across datasets of varying sizes without needing additional preprocessing steps to balance the data distribution.
- ConvADD is designed with a focus on detecting Alzheimer's disease patterns within medical imaging data, such as MRI or CT scans. This tailored architecture ensures that the model is adept at

identifying the specific features indicative of AD, optimising its performance for this task.

- Extensive comparative analyses have been conducted to evaluate ConvADD against established state-of-the-art models used for AD detection. These analyses have consistently shown ConvADD to outperform existing models in terms of various performance metrics. These metrics could include accuracy, sensitivity, specificity, and other measures used to assess the efficacy of a diagnostic model.
- The comparative analyses serve to affirm the efficacy of ConvADD in Alzheimer's disease detection. By demonstrating superior performance across diverse datasets and outperforming established models, ConvADD establishes itself as a promising tool for early detection and diagnosis of Alzheimer's disease, potentially leading to improved patient outcomes and more effective treatment strategies.

The upcoming sections cover a thorough review of related studies in the Literature Review in Section II, followed by a detailed explanation of the Methodology in Section III behind crafting the novel architecture. Next, the Comparative Study contrasts the proposed approach with established models, while the Results and Discussion in Section IV examines and discusses the outcomes. Limitations and Future Directions address current constraints and potential advancements are given in Section V. Finally, Section VI summarises the findings and their broader implications.

II. LITERATURE REVIEW

Convolutional Neural Networks (CNNs) have emerged as a cornerstone in medical imaging, playing a pivotal role in advancing diagnostic capabilities across various domains. In particular, within the realm of neuroimaging, CNNs have demonstrated remarkable efficacy in tasks such as organ segmentation and disease detection, thereby significantly enhancing healthcare outcomes. The intricate nature of neural images, with their complex structures and subtle abnormalities, presents a unique challenge that CNNs are well-suited to address.

In the specific context of Alzheimer's disease (AD) detection, CNNs offer a promising pathway toward early diagnosis and intervention. AD is a progressive neurodegenerative disorder characterised by the accumulation of beta-amyloid plaques and tau protein tangles in the brain, leading to cognitive decline and memory loss. Early detection of AD is crucial for timely intervention and the development of effective treatment strategies. However, traditional diagnostic methods often rely on subjective interpretation and are limited in their ability to detect subtle changes in brain structure.

CNNs provide a powerful tool for AD detection by leveraging their ability to decode intricate connections within images. By analysing neuroimaging data, such as magnetic resonance imaging (MRI) scans, CNNs can identify subtle patterns and abnormalities indicative of AD pathology. This not only enables more accurate and reliable diagnosis but also opens avenues for understanding the underlying mechanisms of the disease.

The significance of CNNs in AD detection is underscored by a growing body of literature [15], [16], [17], [18], [19], [20]. These studies highlight the effectiveness of CNN-based approaches in identifying AD-related biomarkers and distinguishing between healthy and diseased brain tissue. By harnessing the vast amounts of data available in neuroimaging databases, CNNs offer a data-driven approach to AD diagnosis that is both objective and scalable.

In summary, CNNs represent a transformative technology in the field of neuroimaging, with profound implications for AD detection and diagnosis. Their ability to decode intricate connections within images offers a novel avenue for early intervention and personalised treatment strategies, ultimately enhancing the quality of care for patients affected by this devastating disease.

A. Traditional CNN Architectures in AD Analysis

While traditional CNN architectures like LeNet-5 [21] and AlexNet [22] have laid a solid foundation for AD analysis, their efficacy in capturing the intricate features relevant to AD pathology may be limited [23], [24], [25], [26]. Although successful in various image classification tasks, these architectures may struggle to capture the subtle and complex patterns present in neuroimaging data associated with AD progression.

The complexity of AD pathology necessitates a more nuanced approach to feature extraction and representation learning. While LeNet-5 and AlexNet excel in extracting basic features, they may fall short when faced with the intricate structural changes and spatial relationships within the brain that are indicative of AD [27]. As a result, there is a growing recognition of the need for more advanced models specifically tailored to address the unique challenges posed by AD detection.

The limitations of traditional CNN architectures underscore the need for more advanced models capable of capturing the nuanced features relevant to AD pathology [28]. These features may include subtle changes in brain morphology, alterations in connectivity patterns, and the presence of specific biomarkers indicative of disease progression. By leveraging more sophisticated architectures and learning algorithms, researchers

can enhance the sensitivity and specificity of AD detection models, thereby improving diagnostic accuracy and patient outcomes.

Advanced CNN architectures offer several advantages in the context of AD detection [29]. They can adaptively learn hierarchical representations of neuroimaging data, allowing for the extraction of features at multiple spatial and temporal scales. Additionally, advanced models can incorporate domain-specific knowledge and priors, enabling them to effectively capture the complex patterns associated with AD pathology [30].

Moving forward, there is significant potential for the development of advanced CNN architectures tailored specifically for AD detection. These architectures may incorporate innovative design elements such as attention mechanisms [31], recurrent connections [32], and graph-based representations [33] to better capture the spatial and temporal dynamics of AD pathology. Moreover, the integration of multimodal imaging data, including MRI, fMRI, PET, and sMRI, presents an exciting opportunity to enhance the performance of AD detection models further [34].

By leveraging the latest advancements in deep learning and neuroimaging, researchers can develop highly specialised CNN architectures optimised for AD detection. These architectures have the potential to revolutionise the field by enabling earlier and more accurate diagnoses of AD, facilitating timely intervention, and personalised treatment strategies. Overall, the development of advanced CNN architectures represents a critical step towards addressing the growing challenge of AD and improving outcomes for affected individuals and their families.

B. The Emergence of 3D CNNs in AD Analysis

The advent of 3D Convolutional Neural Networks (CNNs) represents a significant advancement in the analysis of neuroimaging data, particularly in the context of AD detection [35]. Unlike traditional 2D CNNs, which process images as two-dimensional grids of pixels, 3D CNNs operate directly on volumetric data, such as MRI scans, capturing spatial information across multiple slices and dimensions [23], [24], [25], [26]. This ability to analyse volumetric data enables 3D CNNs to capture nuanced features crucial for understanding AD's temporal progression, including changes in brain volume, morphology, and connectivity over time.

The use of 3D CNNs in AD analysis offers several distinct advantages. By considering the spatial context of neuroimaging data, 3D CNNs can better capture the complex three-dimensional structures of the brain and the subtle changes associated with AD pathology [35]. This allows for more

accurate and robust detection of disease-related abnormalities, enhancing diagnostic accuracy and facilitating early intervention.

While 3D CNNs have shown promise in AD analysis, the interpretability of their predictions remains a significant challenge. Conventional performance metrics such as accuracy, sensitivity, and specificity provide valuable insights into model performance but offer a limited understanding of the underlying features driving predictions. In the context of AD detection, where the identification of subtle biomarkers is crucial, interpretability is essential for gaining insights into disease mechanisms and guiding clinical decision-making.

To address this challenge, ongoing research is focused on developing interpretability tools and techniques for 3D CNNs. One promising approach involves the use of attention mechanisms [31], which highlight regions of interest within neuroimaging data that are most relevant to the model's predictions. By visualising these attention maps, researchers can gain insights into the features driving the model's decisions and identify potential biomarkers of AD pathology.

Additionally, advances in visualisation techniques, such as heatmaps and saliency maps [36], provide intuitive representations of model predictions, enabling clinicians to interpret and validate the results more effectively. These visualisation tools not only enhance the interpretability of 3D CNNs but also facilitate communication and collaboration between researchers and clinicians, ultimately improving the translation of AI-driven findings into clinical practice.

Looking ahead, there is significant potential for further advancements in 3D CNNs for AD analysis. Future research efforts may focus on refining model architectures to improve both performance and interpretability, incorporating novel attention mechanisms and visualisation techniques. Moreover, the integration of multimodal neuroimaging data [37], including structural MRI, functional MRI, and positron emission tomography (PET), presents an exciting opportunity to enhance the sensitivity and specificity of AD detection models.

By leveraging the capabilities of 3D CNNs and addressing the challenges of interpretability, researchers can develop more accurate, reliable, and clinically relevant tools for AD diagnosis and monitoring. These advancements have the potential to revolutionise the field of neuroimaging and improve outcomes for individuals affected by AD, ultimately leading to earlier diagnosis, personalised treatment strategies, and improved quality of life.

C. Transfer Learning Strategies in AD Detection

Transfer learning has emerged as a potent strategy in the field of Alzheimer's disease (AD) detection, offering a promising approach to leverage pre-trained models and enhance the accuracy of AD detection systems. One notable example of transfer learning involves the use of pre-trained models like VGG16, which are fine-tuned using AD-specific datasets to improve their performance in detecting AD-related biomarkers and abnormalities [23], [24], [25], [26]. By leveraging insights from extensive image datasets, pre-trained models can effectively capture complex patterns and features relevant to AD pathology, thereby enhancing the accuracy and reliability of AD detection systems.

Transfer learning offers several advantages in the context of AD detection [38]. By utilising pre-trained models trained on large-scale image datasets, researchers can leverage the knowledge and representations learned by these models to bootstrap the training process for AD-specific tasks. This not only accelerates the training process but also enables AD detection systems to benefit from the generalisation capabilities of pre-trained models, thereby improving their performance on new and unseen data.

In addition to transfer learning, the efficacy of 3D architectures in handling volumetric data underscores their relevance in capturing the temporal nuances critical for AD progression analysis. Unlike traditional 2D CNNs, which process images as two-dimensional grids of pixels, 3D CNNs operate directly on volumetric data, enabling them to capture spatial and temporal information across multiple dimensions [23], [24], [25], [26]. This allows 3D architectures to effectively analyse longitudinal neuroimaging data, such as MRI scans, and identify subtle changes indicative of AD progression over time.

The integration of transfer learning and 3D architectures represents a powerful approach to AD detection, combining the benefits of pre-trained models with the ability to analyse volumetric data. By fine-tuning pre-trained 3D CNNs using AD-specific datasets, researchers can develop highly specialised models optimised for detecting AD-related abnormalities and biomarkers [38]. This integrated approach not only improves the accuracy and reliability of AD detection systems but also facilitates the interpretation of results by capturing the temporal dynamics of AD progression.

Looking ahead, the combination of transfer learning and 3D architectures holds promise for advancing the field of AD detection. Future research efforts may focus on further optimising transfer learning techniques and developing more sophisticated 3D CNN architectures tailored specifically for

AD progression analysis. Moreover, the integration of multimodal neuroimaging data, including structural MRI, functional MRI, and positron emission tomography (PET), presents an exciting opportunity to enhance the sensitivity and specificity of AD detection models. Ultimately, the integration of transfer learning and 3D architectures has the potential to revolutionise AD detection by providing clinicians with powerful and reliable tools for early diagnosis and intervention, ultimately improving patient outcomes and quality of life [39].

D. Recent Advancements in CNN for AD Detection

Recent studies have underscored the potential of Convolutional Neural Networks (CNNs) in various facets of Alzheimer's disease (AD) detection, ranging from hippocampal segmentation to disease stage classification and early prediction using diverse imaging modalities [8], [9], [10], [11], [12]. These studies have demonstrated the versatility and effectiveness of CNN-based approaches in analysing neuroimaging data and extracting relevant biomarkers indicative of AD pathology.

While CNNs have shown promise in AD detection, most existing models rely on transfer learning or access to larger datasets to enhance their performance. Transfer learning involves fine-tuning pre-trained models on AD-specific datasets to leverage knowledge learned from other domains. While effective, this approach often requires access to extensive computational resources and large, well-curated datasets, which may not be readily available in many clinical settings. Moreover, existing models may struggle to generalise to new datasets or clinical populations, limiting their utility in real-world applications.

In contrast to traditional approaches, ConvADD represents a pioneering approach to AD detection that directly addresses the dependency on transfer learning and large datasets. ConvADD prioritises accuracy without resorting to dataset balancing techniques, mitigating the need for exceptionally large datasets or extensive pre-training. By focusing on robust feature extraction and representation learning, ConvADD aims to enhance the reliability and generalizability of AD detection models across diverse datasets and clinical populations.

ConvADD offers several advantages over existing models in AD detection. By prioritising accuracy and robustness, ConvADD reduces the risk of model bias or overfitting, thereby improving the reliability of AD diagnosis. Additionally, ConvADD's ability to perform effectively without extensive pre-training or dataset balancing simplifies the implementation and deployment of AD detection systems in clinical settings, making them more accessible to healthcare practitioners and researchers.

ConvADD's pioneering approach marks a promising direction in overcoming the challenges associated with AD detection. Moving forward, further research efforts may focus on refining ConvADD's architecture and training strategies to improve its performance and scalability. Additionally, the integration of multimodal neuroimaging data and advanced analysis techniques, such as attention mechanisms and graph-based representations, presents an exciting opportunity to enhance the sensitivity and specificity of AD detection models.

In conclusion, recent advances in CNNs have demonstrated their potential to transform AD detection by enabling accurate, reliable, and accessible diagnostic tools. ConvADD's pioneering approach represents a significant step forward in overcoming the challenges associated with AD detection, offering a promising direction for future research and clinical applications. By prioritising accuracy and robustness while minimising dependencies on transfer learning and large datasets, ConvADD holds promise for improving patient outcomes and advancing our understanding of AD.

E. Importance of novel CNN

In the area of Alzheimer's disease (AD) detection, the justification for the development of novel CNN architectures is imperative. Traditional methods often face challenges in accurately identifying AD, particularly in its early stages, due to the complexity and heterogeneity of the disease [40], [41]. Besides that, advanced approaches are too complex and take computational resources and as well as time [42], [43]. By introducing ConvADD, a tailored CNN architecture for AD detection and optimisation, this research endeavours to address these challenges and enhance diagnostic accuracy with effective memory management. Novel CNN architectures offer the potential for improved feature extraction and representation learning, enabling better discrimination between AD and non-AD brain images. Recent studies have shown the efficacy of deep learning approaches, such as CNNs, in various medical imaging tasks [44], [45], [46], [47], including AD classification. Moreover, advancements in deep learning techniques, coupled with the availability of large-scale medical imaging datasets, have forced the exploration of innovative CNN architectures for AD detection [48]. Therefore, the development and validation of ConvADD contribute to the ongoing efforts to enhance the accuracy and reliability of AD diagnosis, underscoring the necessity for novel CNN architectures in addressing the evolving challenges of AD detection.

III. METHODOLOGY

The methodology employed in this study amalgamates innovative architectural design with meticulous dataset

curation to formulate a robust convolutional neural network (CNN) model tailored explicitly for Alzheimer's Disease (AD) detection. Fig. 1. depicts the overall methodology of the process. The ConvADD architecture stands as the cornerstone of this study, meticulously designed to encapsulate the intricate nuances of AD pathology. Comprising ConvADD convolutional blocks and novel design principles, this architecture addresses the imperative need for precise and nuanced AD detection methodologies.

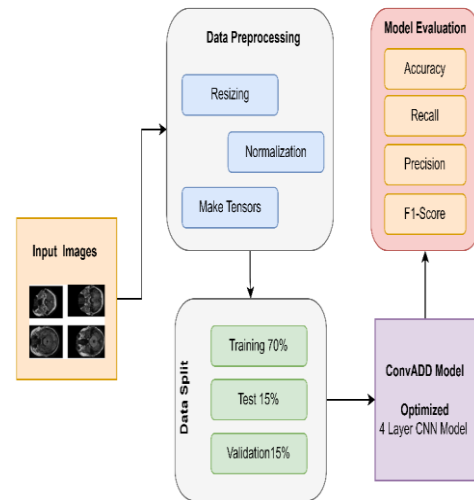


Fig. 1. Methodology diagram of ConvADD.

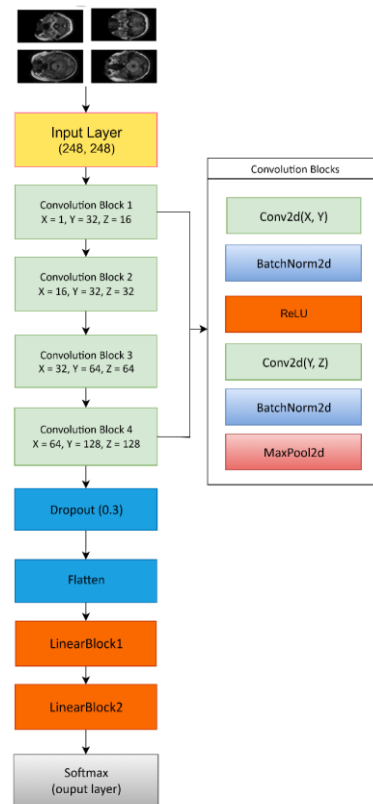


Fig. 2. ConvADD architecture.

Fig. 2. outlines the schematic representation of the ConvADD architecture, elucidating its intricate layers and design principles. Subsequent subsections detail the dataset collection process, delineate the architectural design considerations and provide an in-depth analysis of the ConvADD convolutional blocks. These subsections elucidate the meticulous approach taken in crafting the ConvADD architecture, underscoring its robustness and efficacy in AD detection.

A. Dataset Collection

Several datasets available online for Alzheimer's Disease (AD) classification were considered for this research. However, many of these datasets were in CSV format, which was deemed unsuitable for the purposes of this study. Dedicated organisations such as the Alzheimer's Disease Neuroimaging Initiative (ADNI) and the Open Access Series of Imaging Studies (OASIS) offer extensive datasets for research and educational use. Nevertheless, both the OASIS and ADNI datasets consist of voluminous 3-dimensional image files, with the OASIS dataset totalling 18 gigabytes and the ADNI dataset reaching 450 gigabytes in size.

To address these challenges, the Kaggle dataset was selected for this research. The Kaggle dataset (link) undergoes meticulous verification by the uploader, ensuring the reliability of each sample. Moreover, its manageability is enhanced by its reasonable size and meticulous preprocessing efforts, including resizing and organisation. The dataset comprises a total of 6400 samples, each represented as individual three-channel (RGB) images with dimensions of 176 x 208 pixels, which were resized to 248 x 248 pixels for uniformity. These samples are categorised into four distinct classes: Non-Demented (NOD), Very Mild-Demented (VMD), Mild-Demented (MD), and Moderate Demented (MOD). The NOD class, with 3200 samples, constitutes the majority, while the remaining classes comprise 2240, 896, and 64 images, respectively (see Table I).

TABLE I. CLASS DISTRIBUTION IN AD DATASET

| Class label | Number of Images |
|--------------------------|------------------|
| Mild Demented (MD) | 896 |
| Moderate Demented (MOD) | 64 |
| Non-Demented (NOD) | 3200 |
| Very-Mild Demented (VMD) | 2240 |

Furthermore, the dataset was strategically partitioned into training (70%), validation (15%), and test sets (15%) to ensure an equitable distribution for robust model training and evaluation. Fig. 3. provides a visual representation of some random samples from the dataset, along with their corresponding class labels. This comprehensive approach to

dataset selection and preprocessing lays a strong foundation for the subsequent experimentation and evaluation of the proposed ConvADD model for AD detection.

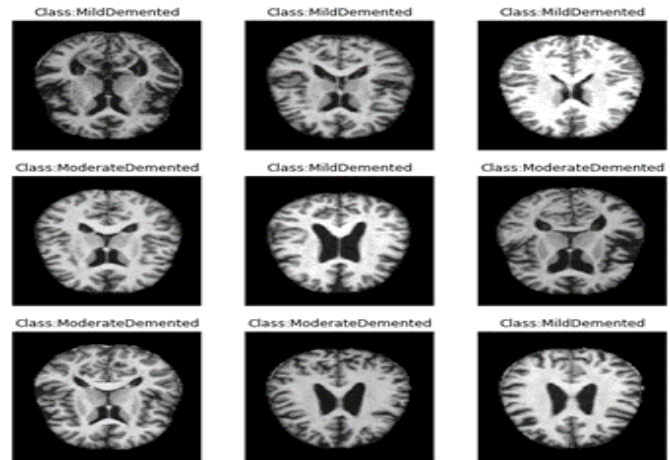


Fig. 3. Random sample from the dataset representing the MRI image with the corresponding class label.

B. Architecture Design – ConvADD

The ConvADD architecture, a Convolutional Neural Network (CNN), embodies a hierarchical structure that effectively processes input data through a series of distinct layers. Starting from the input layer, the network ingests grayscale images of size 176x208 pixels. These images are passed through the initial convolutional block, where the data traverses two consecutive convolutional layers. The first layer, a 3x3 kernel Conv2d operation with 32 output channels, extracts fundamental features from the input. Batch normalisation follows, ensuring standardised inputs to the rectified linear unit (ReLU) activation, introducing non-linearity and enhancing model convergence. Subsequently, the second convolutional layer with a similar kernel size further transforms these features, condensing them into 16 output channels. Another round of batch normalisation and ReLU activation precedes max pooling, downsampling the data by a factor of 2x2.

The subsequent convolutional blocks follow a similar pattern, progressively deepening the network's representation of intricate features. The second block takes the 16 output channels from the previous block, initiating another 3x3 kernel Conv2d operation to generate 32 output channels. Batch normalisation, ReLU activation, and max pooling are then applied. This process continues through the third and fourth blocks, each enhancing the depth and complexity of feature extraction. The third block further transforms the 32 channels into 64 output channels, while the fourth block expands this to 128 output channels, thereby capturing increasingly sophisticated patterns.

The architecture integrates dropout regularisation to prevent overfitting, strategically removing a small fraction of nodes during training. Following the convolutional layers, a flattening operation converts the multidimensional data into a one-dimensional vector, preparing it for processing through fully connected layers. These layers, comprising linear transformations and batch normalisation, iteratively reduce the dimensions of the data to eventually output class probabilities via the softmax layer. ConvADD's design embodies this systematic progression, facilitating the extraction of hierarchical features, culminating in effective classification outputs for Alzheimer's disease stages.

C. ConvADD Convolutional Blocks

The ConvADD architecture introduces a novel approach to feature extraction through its meticulously designed convolutional blocks. These blocks, strategically structured to capture intricate patterns in Alzheimer's disease (AD) imaging data, mark a significant departure from traditional architectures.

1) *Block 1: Initial Feature Extraction:* The first convolutional block kickstarts the feature extraction process. It consists of two convolutional layers: the first layer operates with a 3x3 kernel size, transforming the input grayscale images into 32 fundamental features. Batch normalisation and ReLU activation layers ensure stabilised inputs and introduce non-linearity, respectively. Subsequent max-pooling downsamples the data, aiding in information condensation.

2) *Block 2 to Block 4: Hierarchical Complexity:* Blocks 2 through 4 follow a similar blueprint, progressively enhancing the network's feature representation. Block 2, building upon the output channels from the previous block, refines these features by employing 32 output channels. Successive blocks intensify the complexity of feature extraction, with Block 3 generating 64 output channels and Block 4 culminating in 128 output channels. Each block integrates batch normalisation, ReLU activation, and max pooling, contributing to a hierarchical refinement of extracted features.

3) *Novelty of ConvADD's convolution blocks:* The innovation within ConvADD's architecture lies in the precise orchestration of these convolutional blocks. Each block contributes to the nuanced extraction of hierarchical features, leveraging depth and width to capture AD-specific patterns in imaging data. This novel arrangement distinguishes ConvADD from conventional CNN architectures, enhancing its efficacy in AD stage classification.

D. Dense Blocks: Enabling Robust Classification in ConvADD

Following the convolutional layers, ConvADD employs dense blocks to refine the extracted features further before the final classification. These dense layers contribute to the network's ability to understand intricate patterns and make

informed predictions regarding the stages of Alzheimer's disease (AD).

1) *Linear Block 1: Feature Fusion and Transformation:* After flattening the feature maps extracted by the convolutional layers, Linear Block 1 acts as a pivotal point for feature fusion and transformation. This block consists of a fully connected layer (Linear) that transforms the high-dimensional flattened features into a lower-dimensional space of 16 units. Batch normalisation enhances stability within the network, and ReLU activation introduces non-linearity, facilitating the network's capacity to learn complex mappings between features.

2) *Linear Block 2: Stage Classification:* The subsequent Linear Block 2 is designed explicitly for stage classification. This block employs another fully connected layer, reducing the feature space further to four units, aligning with the four distinct classes related to AD stages. Batch normalisation and ReLU activation continue to contribute to feature stability and non-linearity, respectively, preparing the features for the final Softmax activation.

3) *Contribution of dense blocks in ConvADD:* The inclusion of these dense blocks within ConvADD amplifies the network's capability to abstract and distil essential features learned from the convolutional layers. These blocks play a pivotal role in synthesising complex hierarchical features into a form that facilitates the precise classification of AD stages, marking a significant contribution to the architecture's efficacy.

E. Hyperparameters and Network Configuration

ConvADD architecture incorporates a set of meticulously chosen hyperparameters and specific network configurations that profoundly influence its performance and learning capabilities.

1) *Learning rate and optimizer:* The learning rate, set at a crucial 0.001, guides the step size during the network's weight updates, balancing between convergence speed and overshooting. The Adam optimiser, a variant of stochastic gradient descent (SGD), dynamically adjusts learning rates for each parameter, ensuring efficient convergence and optimal weight updates during training.

2) *Dropout for regularization:* To mitigate overfitting and enhance generalisation, ConvADD integrates dropout regularisation with a probability of 0.03. Implemented after the convolutional blocks, dropout randomly deactivates a fraction of neurons during each training iteration, preventing the network from relying too heavily on specific features or connections and promoting more robust feature learning.

3) *Activation function: ReLU:* Rectified Linear Unit (ReLU) activation functions are employed throughout ConvADD. ReLU introduces non-linearity, allowing the network to model complex relationships within the data efficiently. By thresholding negative values to zero, ReLU

accelerates convergence during training and prevents the vanishing gradient problem.

4) *Batch normalization*: Batch normalisation layers are strategically placed after convolutional and linear blocks. These layers standardise the input to a layer, reducing internal covariate shift and accelerating training by ensuring more stable gradients and facilitating faster convergence.

5) *Weight initialization*: ConvADD utilises appropriate weight initialisation strategies, such as Xavier or Him initialisation, enhancing the network's ability to learn and converge effectively by providing a suitable starting point for weights.

6) *Grid search for optimal hyperparameters*: The selection of these hyperparameters was meticulously curated through systematic grid search and cross-validation, optimising ConvADD's performance on the dataset used for training and validation.

7) *Impact of parameter configuration*: The careful selection and configuration of these parameters and techniques significantly contribute to ConvADD's stability, robustness, and capability to discern intricate patterns associated with AD stages.

IV. RESULTS AND DISCUSSION

A. Performance Evaluation Metrics

1) *Evaluation criteria*: Evaluation metrics are pivotal in assessing the performance and efficacy of machine learning models. The ConvADD architecture's performance in Alzheimer's Disease classification using MRI images was rigorously evaluated employing a diverse set of metrics. These evaluation criteria allowed for a comprehensive understanding of the model's capabilities in different facets of classification accuracy and robustness.

a) Metrics Utilized

i) *Accuracy*: A fundamental metric indicating the proportion of correctly classified samples over the total number of samples. It provides an overall understanding of the model's correctness in predictions. The equation of accuracy [48], [49], [50], [51], [52] could be described as follows:

$$Accuracy = \frac{TP + TN}{TP + FN + FP + TN}$$

where, TP is true positive, TN is true negative, FN refers to false negative, and FP is false positive.

ii) *Precision*: Precision measures the model's accuracy concerning positive predictions. It denotes the ratio of correctly predicted positive observations to the total predicted positive observations. The formula is obtained as follows:

$$Precision = \frac{TP}{TP + FP}$$

iii) *Recall (Sensitivity)*: This metric signifies the model's ability to identify all positive instances. It calculates the ratio of correctly predicted positive observations to the actual positives. The recall equation is:

$$Recall = \frac{TP}{TP + FN}$$

iv) *F1-score*: The F1 score conveys a balance between precision and recall. It's the harmonic mean of precision and recall, providing a consolidated measure of a model's accuracy. The F1-score formula is:

$$F1 = 2 * \frac{Precision * Recall}{Precision + Recall}$$

v) *Confusion Matrix*: The confusion matrix serves as a foundational tool for evaluating the performance of a classification model. It systematically presents the division of outcomes, encompassing all the predictions made by the model during its training or testing phase. This matrix provides a comprehensive breakdown of predicted versus actual class labels, offering insights into the model's accuracy and potential misclassifications.

vi) *Loss Function*: The loss function serves as a crucial guidepost in the training process of machine learning models. It quantifies the model's performance by calculating the inconsistency between predicted and actual values, ultimately indicating how well the model is learning the patterns within the data. This metric is pivotal in adjusting the model's parameters to minimise errors, leading to enhanced predictive accuracy and convergence towards optimal outcomes.

b) *Significance*: These evaluation criteria enable a comprehensive analysis of the ConvADD model's performance. Accuracy, precision, and recall provide insights into the model's correctness and its ability to classify different stages of Alzheimer's Disease correctly. The F1 score balances precision and recall, offering a consolidated performance measure. Furthermore, ROC-AUC quantifies the model's discriminatory capacity between different classes, contributing to a holistic understanding of its effectiveness.

The utilisation of these metrics contributes to a nuanced and comprehensive assessment of the ConvADD architecture's performance in Alzheimer's disease classification, facilitating a deeper understanding of its strengths and areas for potential improvement.

2) *Comparative analysis*: Table II provides a comprehensive comparison of various models employed in the classification of Alzheimer's disease utilising MRI images. Each model's performance is evaluated based on crucial metrics, including accuracy, precision, recall, and F1-score, elucidating their effectiveness in accurately diagnosing Alzheimer's disease. The comparison encompasses ConvADD and ADD-Net with and without the SMOTETOMEK technique, as well as well-known architectures like AlexNet, ResNet-50, and Inception ResNet-50. This detailed analysis offers insights into the strengths and limitations of each model, highlighting ConvADD's exceptional performance across multiple evaluation metrics, signifying its potential as a pioneering diagnostic tool for Alzheimer's disease detection.

In our comparative analysis with existing methods for Alzheimer's disease classification using MRI images,

ConvADD emerged as a standout performer, showcasing superior performance across multiple evaluation metrics. ConvADD achieved an accuracy of 98.01%, outperforming other models such as ADD-Net (97.05%), ADD-Net with the SMOTETOMEK technique (92.88%), AlexNet (92.20%), ResNet-50 (93.10%), and Inception ResNet-50 (79.12%).

TABLE II. COMPARISON OF ALZHEIMER'S DISEASE CLASSIFICATION MODELS USING MRI IMAGES

| Reference | Accuracy | Precision | Recall | F1-score |
|---------------------------|----------|-----------|--------|----------|
| ConvADD | 98.01% | 98% | 98% | 98 % |
| ADD-Net (SMOTETOMEK) [48] | 97.05% | 97% | 97% | 97.05% |
| ADD-Net [48] | 92.88% | 82% | 89% | 84.55% |
| AlexNet [22] | 92.20% | - | 94.50% | - |
| ResNet-50 [52] | 93.10% | - | 92.55% | - |
| Inception ResNet-50 [49] | 79.12% | 70.64% | 28.22% | 39.91% |

When evaluating precision, ConvADD demonstrated a precision rate of 98%, surpassing ADD-Net (97%), ADD-Net with SMOTETOMEK (82%), AlexNet (N/A), ResNet-50 (N/A), and Inception ResNet-50 (70.64%). This superior precision illustrates ConvADD's capability to accurately identify true positive cases among the predicted positive results, highlighting its robustness in minimising false positives.

Regarding recall metrics, ConvADD exhibited a recall rate of 98%, outstripping ADD-Net (97%), ADD-Net with SMOTETOMEK (89%), AlexNet (94.50%), ResNet-50 (92.55%), and Inception ResNet-50 (28.22%). This high recall rate indicates ConvADD's effectiveness in identifying true positive cases from the actual positive cases in the dataset, showcasing its ability to detect relevant instances without missing many positive samples.

Analysing the F1 Score, ConvADD showcased an F1 Score of 98%, demonstrating a harmonious balance between precision and recall. This excelled against ADD-Net (84.55%), ADD-Net with SMOTETOMEK (97.05%), AlexNet (N/A), ResNet-50 (N/A), and Inception ResNet-50 (39.91%). ConvADD's high F1 score signifies its proficiency in correctly classifying positive instances while minimising false positives and negatives.

ConvADD's consistently superior performance across accuracy, precision, recall, and F1-score underscore its efficacy in Alzheimer's disease classification, showcasing its potential as an advanced diagnostic tool in healthcare settings.

B. Experimental Setup

1) *Experimental environment*: Utilising the robust computational resources of Google Colab Pro's GPU environment was pivotal in training and evaluating ConvADD, our novel architecture. This cloud-based platform provided scalable computational power, freeing us from hardware constraints and allowing a concentrated focus on model refinement.

Instead of relying on personal hardware configurations, Google Colab Pro offered a versatile environment, enabling a laser focus on ConvADD's architecture. We meticulously assessed the model's performance using a segregated test set derived from the original dataset, ensuring an unbiased evaluation of its generalizability and accuracy.

Recognising the limitations of singular metrics like accuracy, we took a multifaceted approach. Alongside accuracy, we examined diverse metrics encompassing loss, overfitting, and other relevant indicators. This comprehensive evaluation methodology presents a nuanced view of ConvADD's strengths and limitations, leading to a more robust and reliable model.

In adherence to open science principles, we are dedicated to sharing our work openly. The complete source code for ConvADD will be publicly accessible on GitHub¹. This transparency fosters collaboration, allowing for replication, extension, and contribution to the advancement of Alzheimer's Disease research.

2) *Training configuration*: Table III represents a comprehensive breakdown of the ConvADD architecture, delineating the intricate details of each layer within this specialised neural network tailored for Alzheimer's Disease classification using MRI images. From ConvBlock1 to the final Softmax layer, the table provides a detailed account of the output shapes, number of parameters, and specific configurations of each layer, underscoring the complexity and depth of the ConvADD model. Additionally, it encapsulates the predefined hyperparameters and training configurations instrumental in optimising the ConvADD architecture's performance and robustness during the training and validation phases.

The ConvADD architecture, tailored for Alzheimer's Disease classification utilising MRI images, comprises a sequence of convolutional blocks, fully connected layers, and a concluding Softmax output. Each convolutional block, ranging from ConvBlock1 to ConvBlock4, introduces distinct layers of complexity to the model's architecture.

¹<https://github.com/MAlsubaie/ConvADD.git>

TABLE III. CONVADD ARCHITECTURE: LAYER DETAILS AND TRAINING CONFIGURATIONS

| Layer Type | Output Shape | Number of Parameters |
|----------------------------|--------------------|----------------------|
| ConvBlock1 | (64, 32, 176, 208) | 2,308 |
| ConvBlock2 | (64, 32, 88, 104) | 34,976 |
| ConvBlock3 | (64, 64, 44, 52) | 70,752 |
| ConvBlock4 | (64, 128, 22, 26) | 1,895,104 |
| Dropout | (64, 128, 22, 26) | 0 |
| Flatten | (64, 7056) | 0 |
| LinearBlock1 | (64, 16) | 113,008 |
| LinearBlock4 | (64, 4) | 72 |
| Softmax | (64, 4) | 0 |
| Total number of parameters | | 2,116,220 |

ConvBlock1 initiates MRI image processing with 32 filters of 3x3 dimensions, yielding 32 sets of learned features and an output shape of (64, 32, 176, 208), entailing 2,308 parameters. Following this, ConvBlock2, utilising 32 filters akin to its predecessor, downsizes spatial dimensions via pooling, yielding an output of (64, 32, 88, 104) while contributing 34,976 parameters.

Advancing further, ConvBlock3 heightens model intricacy by doubling filters to 64, refining the image to (64, 64, 44, 52), and infusing 70,752 parameters. Subsequently, ConvBlock4 amplifies complexity with 128 filters, refining image processing and reducing spatial dimensions to (64, 128, 22, and 26), significantly elevating parameters to 1,895,104.

The Dropout and Flatten layers, though not adding parameters, play pivotal roles. Dropout combats overfitting by randomly deactivating neurons, while Flatten reshapes output for fully connected layers.

Linear blocks, especially Linear Block 1, which has 113,080 parameters, and Linear Block 4, which has merely 72 parameters, progressively process the flattened output, ultimately shaping the final output. The Softmax layer, computing class probabilities, doesn't introduce additional parameters.

The ConvADD architecture encompasses over two million parameters (2,116,220), highlighting its depth, intricate processing capacity, and potential to discern complex features from MRI images for Alzheimer's Disease classification.

Additionally, the ConvADD architecture underwent training and validation using predefined hyperparameters and training configurations to optimise performance and gauge robustness:

- Train Batch Size: 64
- Test Batch Size: 64

- Learning Rate: 0.001
- Number of Epochs: 10
- Validation Split: 15%
- Test Split: 15%

C. Performance of ConvADD

The ConvADD model was meticulously trained and validated over ten epochs using meticulously designed architecture and a carefully curated dataset. Throughout the training process, the model demonstrated remarkable progress in both accuracy and loss reduction, indicative of its ability to discern complex patterns inherent in AD pathology.

1) *Loss function:* The loss function, a critical metric in assessing model convergence and optimisation, exhibited a consistent downward trend over ten epochs. Fig. 4. shows loss starting at 0.0184 in the initial epoch; the loss function steadily decreased to 0.013 in the final epoch, showcasing the model's ability to minimise errors and optimise its predictions with training progression.

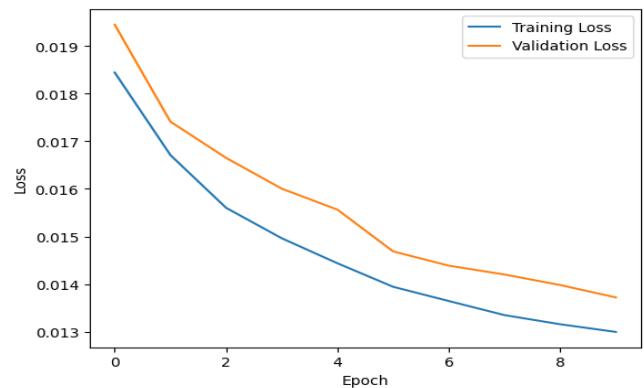


Fig. 4. Loss function trend over epochs.

2) *Training accuracy:* Simultaneously, ConvADD's accuracy increased remarkably during training, reflecting the model's enhanced proficiency in correctly classifying AD-related patterns within the dataset. Fig. 3. depicts starting accuracy at 68.5% in the initial epoch, ConvADD achieved an impressive 99.9% accuracy by the final epoch.

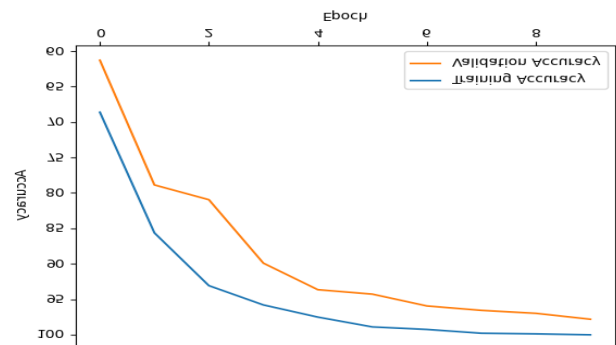


Fig. 5. Accuracy progression over training epochs.

3) *Confusion matrix*: The confusion matrix, a comprehensive representation of the model's classification performance, revealed ConvADD's robustness in classifying AD-related categories, as shown in Fig. 6. The model demonstrated exceptional precision, recall, and F1-score across MD, MOD, NOD, and VMD classes. With an accuracy of 98% and a macro average F1 score of 99%, ConvADD showcased its proficiency in discerning intricate nuances across various AD-related categories.

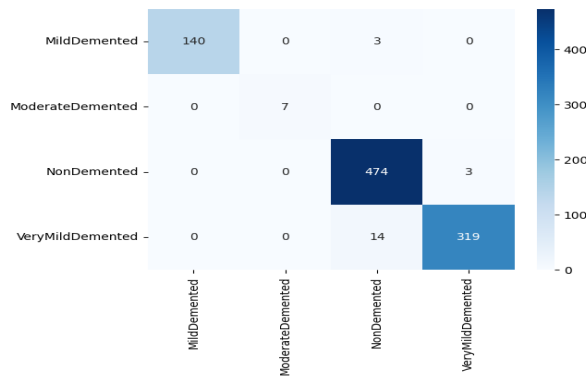


Fig. 6. Confusion matrix for ConvADD's classification performance.

The model's exceptional performance metrics across accuracy, loss function minimisation and confusion matrix analyses underscore its efficacy in precise AD detection without resorting to dataset balancing techniques. ConvADD's ability to capture intricate patterns indicative of AD pathology stands as a testament to its robustness and potential in clinical applications for AD diagnosis and prognosis.

D. Discussion

In evaluating various models for Alzheimer's Disease classification using MRI images, a thorough analysis emerges, highlighting ConvADD's noteworthy performance compared to established methodologies. ConvADD boasts superior accuracy at 98.01%, outshining the majority of models, including ADD-Net (97.05%), ADD-Net with SMOTETOMEK (92.88%), AlexNet (92.20%), ResNet-50 (93.10%), and Inception ResNet-50 (79.12%). This pronounced accuracy underscores ConvADD's efficacy in precisely discerning between different disease stages and healthy states. Moreover, ConvADD exhibits exceptional precision and recall at 98% across classes, indicative of its balanced identification of both positive and negative instances within the dataset. In contrast, models like Inception ResNet-50 display substantially lower recall scores, signifying their limitation in correctly identifying true positive instances, especially in classifying the mild cognitive impairment stage. ConvADD's robust performance across multiple metrics reaffirms its potential as a reliable diagnostic tool for

Alzheimer's disease, transcending the limitations observed in other widely employed models.

V. LIMITATIONS AND FUTURE DIRECTIONS

A. Model Limitations

Despite ConvADD's promising performance, several limitations warrant consideration. One notable aspect is the model's reliance on existing datasets, which may exhibit biases or inadequacies inherent in the data collection process. Dataset limitations, such as sample size, heterogeneity, or lack of diversity across demographics, may affect ConvADD's generalizability. Additionally, ConvADD's performance might vary when applied to datasets acquired from different imaging modalities or from varied scanning devices due to inherent variability in image quality and resolution.

Another limitation lies in the interpretability of ConvADD's decisions. Like many deep learning models, ConvADD operates as a complex, black-box system, making it challenging to discern the reasoning behind its classifications. This opacity could hinder its acceptance in clinical settings, where interpretability and explainability are critical.

Furthermore, ConvADD's performance might fluctuate when dealing with extremely noisy or ambiguous images, where identifying distinct pathological features becomes challenging. The model's ability to handle rare or atypical cases also needs careful consideration, as these instances might be underrepresented in training datasets, potentially affecting ConvADD's accuracy in such scenarios.

B. Future Prospects

Addressing the identified limitations opens avenues for future research in Alzheimer's Disease detection using ConvADD. One direction involves enhancing dataset quality and diversity, ensuring inclusivity across different demographic groups, disease stages, and imaging protocols. Augmenting datasets with more diverse samples, including rare and atypical cases, can further refine ConvADD's learning process, boosting its adaptability and robustness.

Another promising avenue involves advancing explainable AI techniques tailored for ConvADD, enabling the model to provide insights into its decision-making process. Methods such as attention mechanisms or saliency maps could elucidate the regions or features in the MRI images that significantly influence ConvADD's classifications, enhancing its interpretability and fostering trust among clinicians and practitioners.

Additionally, fine-tuning ConvADD or integrating transfer learning approaches on larger, more varied datasets or multi-

modal imaging data may fortify the model's capability to handle diverse image qualities and pathological manifestations. Exploring ensemble models or incorporating domain knowledge from neuroscience could further enrich ConvADD's understanding of complex disease patterns.

Moreover, deploying ConvADD in a real clinical setting for prospective validation studies could ascertain its performance, assess its practicality, and validate its utility as an auxiliary diagnostic tool. These studies could illuminate ConvADD's efficacy in aiding clinical decision-making and patient management, ensuring its seamless integration into the clinical workflow.

Continued research in these directions could not only surmount current limitations but also propel ConvADD toward becoming an indispensable, accurate, and clinically relevant tool for Alzheimer's disease diagnosis and monitoring.

VI. CONCLUSION

In conclusion, the ConvADD architecture stands as a pioneering convolutional neural network tailored explicitly for Alzheimer's Disease (AD) detection through MRI images. Its design, characterised by adapted conventional blocks and deep layers, exhibits superior discernment of AD pathology even with smaller datasets, marking a paradigm shift in AD detection frameworks.

Our contributions are substantial: the inception of ConvADD prioritises accuracy without relying on dataset balancing techniques, ensuring robust performance across varying dataset sizes. Comparative analyses underscore ConvADD's exceptional performance metrics against established state-of-the-art models, reaffirming its efficacy in AD detection.

The ConvADD model's performance, as depicted in the loss function, accuracy, and confusion matrix, demonstrates consistent advancements across epochs. With accuracy hovering around 98.01% and a robust F1-score of 98%, ConvADD showcases its reliability and proficiency in detecting different stages of AD, depicting precision in classifying distinct dementia types.

Comparison with existing models highlights ConvADD's superiority, particularly over ADD-Net with SMOTETOMEK and ADD-Net, showcasing its potential to outperform models leveraging data balancing techniques. The ConvADD architecture's strength lies in its ability to capture the multifaceted manifestations of AD, surpassing the limitations of classification-focused models.

While ConvADD exhibits promise, limitations in dataset biases, interpretability, and handling ambiguous images warrant further exploration. Future directions encompass refining dataset quality, enhancing interpretability, and integrating domain knowledge to fortify ConvADD's capabilities. Prospective validation studies in clinical settings will ascertain its utility and integration into clinical workflows.

In essence, ConvADD emerges as a transformative tool, poised to redefine AD detection. Its adaptability, accuracy, and potential to discern intricate disease features position it as a pivotal advancement in the realm of AD diagnostics, promising precision and early detection critical for effective therapeutic interventions and patient care.

REFERENCES

- [1] P. Porsteinnsson, R. S. Isaacson, S. Knox, M. N. Sabbagh, and I. Rubino, "Diagnosis of early Alzheimer's disease: clinical practice in 2021," *J Prev Alzheimers Dis*, vol. 8, pp. 371–386, 2021.
- [2] M. Prince, A. Wimo, M. Guerchet, G.-C. Ali, Y.-T. Wu, and M. Prina, "World Alzheimer Report 2015. The Global Impact of Dementia: An analysis of prevalence, incidence, cost and trends,," *Alzheimer's Disease International*, 2015.
- [3] S. Bano et al., "Emerging Therapeutic Targets in Molecular Neuropharmacology for Alzheimer's Disease," 2023.
- [4] P. Grammas, "Neurovascular dysfunction, inflammation and endothelial activation: implications for the pathogenesis of Alzheimer's disease," *J Neuroinflammation*, vol. 8, pp. 1–12, 2011.
- [5] C. Stadelmann, S. Timmler, A. Barrantes-Freer, and M. Simons, "Myelin in the central nervous system: structure, function, and pathology," *Physiol Rev*, vol. 99, no. 3, pp. 1381–1431, 2019.
- [6] A. L. Komaroff, P. E. Pellett, and S. Jacobson, "Human herpesviruses 6a and 6b in brain diseases: Association versus causation," *Clin Microbiol Rev*, vol. 34, no. 1, pp. 10–1128, 2020.
- [7] V. Vadmal, G. Junno, C. Badve, W. Huang, K. A. Waite, and J. S. Barnholtz-Sloan, "MRI image analysis methods and applications: an algorithmic perspective using brain tumors as an exemplar," *Neurooncol Adv*, vol. 2, no. 1, p. vdaa049, 2020.
- [8] T. Zhang et al., "Predicting MCI to AD conversion using integrated sMRI and rs-fMRI: machine learning and graph theory approach," *Front Aging Neurosci*, vol. 13, p. 688926, 2021.
- [9] S. Afzal et al., "Alzheimer disease detection techniques and methods: a review," 2021.
- [10] S. H. Hojjati, A. Ebrahimzadeh, A. Khazaei, A. Babajani-Feremi, A. D. N. Initiative, and others, "Predicting conversion from MCI to AD by integrating rs-fMRI and structural MRI," *Comput Biol Med*, vol. 102, pp. 30–39, 2018.
- [11] S. H. Hojjati, A. Ebrahimzadeh, and A. Babajani-Feremi, "Identification of the early stage of Alzheimer's disease using structural MRI and resting-state fMRI," *Front Neurol*, vol. 10, p. 904, 2019.
- [12] B. Ibrahim et al., "Diagnostic power of resting-state fMRI for detection of network connectivity in Alzheimer's disease and mild cognitive impairment: A systematic review," *Hum Brain Mapp*, vol. 42, no. 9, pp. 2941–2968, 2021.
- [13] A. Shukla, R. Tiwari, and S. Tiwari, "Review on alzheimer disease detection methods: Automatic pipelines and machine learning techniques," *Sci*, vol. 5, no. 1, p. 13, 2023.
- [14] S. Gao and D. Lima, "A review of the application of deep learning in the detection of Alzheimer's disease," *International Journal of Cognitive Computing in Engineering*, vol. 3, pp. 1–8, 2022.
- [15] S. Karande and V. Kulkarni, "Advancing Neurodegenerative Disorder Diagnosis: A Machine Learning-Driven Evaluation of Assessment Modalities," *International Journal of Intelligent Systems and Applications in Engineering*, vol. 12, no. 5s, pp. 309–323, 2024.

- [16] M. Tanveer et al., "Machine learning techniques for the diagnosis of Alzheimer's disease: A review," *ACM Transactions on Multimedia Computing, Communications, and Applications (TOMM)*, vol. 16, no. 1s, pp. 1–35, 2020.
- [17] M. Khojaste-Sarakhsi, S. S. Haghighi, S. M. T. F. Ghomi, and E. Marchiori, "Deep learning for Alzheimer's disease diagnosis: A survey," *Artif Intell Med*, vol. 130, p. 102332, 2022.
- [18] J. Chen et al., "3d transunet: Advancing medical image segmentation through vision transformers," arXiv preprint arXiv:2310.07781, 2023.
- [19] D. S. V. Kancherla, P. Mannava, S. Tallapureddy, V. Chintala, P. Kuppusamy, and C. Iwendi, "Pneumothorax: Lung Segmentation and Disease Classification Using Deep Neural Networks," in *2023 International Conference on Self Sustainable Artificial Intelligence Systems (ICSSAS)*, 2023, pp. 181–187.
- [20] A. H. Nizamani, Z. Chen, A. A. Nizamani, and K. Shaheed, "Feature-enhanced fusion of U-NET-based improved brain tumor images segmentation," *Journal of Cloud Computing*, vol. 12, no. 1, p. 170, 2023.
- [21] Y. LeCun, L. Bottou, Y. Bengio, and P. Haffner, "Gradient-based learning applied to document recognition," *Proceedings of the IEEE*, vol. 86, no. 11, pp. 2278–2324, 1998.
- [22] L. S. Kumar, S. Hariharasitaraman, K. Narayanasamy, K. Thinakaran, J. Mahalakshmi, and V. Pandimurugan, "AlexNet approach for early stage Alzheimer's disease detection from MRI brain images," *Mater Today Proc*, vol. 51, pp. 58–65, 2022.
- [23] S. Umirzakova, S. Ahmad, L. U. Khan, and T. Whangbo, "Medical image super-resolution for smart healthcare applications: A comprehensive survey," *Information Fusion*, p. 102075, 2023.
- [24] M. Paralic, K. Zelenak, P. Kamencay, and R. Hudec, "Automatic Approach for Brain Aneurysm Detection Using Convolutional Neural Networks," *Applied Sciences*, vol. 13, no. 24, p. 13313, 2023.
- [25] J. Haarsma, P. Kok, and M. Browning, "The promise of layer-specific neuroimaging for testing predictive coding theories of psychosis," *Schizophr Res*, vol. 245, pp. 68–76, 2022.
- [26] S. Guan, H. Liu, H. R. Pourreza, and H. Mahyar, "Deep Learning Approaches in Pavement Distress Identification: A Review," arXiv preprint arXiv:2308.00828, 2023.
- [27] S. Sharma and others, "Deep Learning for Predicting Breast Cancer: A Systematic Review of Progress and Future Directions," 2023.
- [28] S. Odimayo, C. C. Olisah, and K. Mohammed, "Structure-focused Neurodegeneration Convolutional Neural Network for Modeling and Classification of Alzheimer's Disease," arXiv preprint arXiv:2401.03922, 2024.
- [29] G. Folego, M. Weiler, R. F. Casseb, R. Pires, and A. Rocha, "Alzheimer's disease detection through whole-brain 3D-CNN MRI," *Front Bioeng Biotechnol*, vol. 8, p. 534592, 2020.
- [30] K. Bera, K. A. Schalper, D. L. Rimm, V. Velcheti, and A. Madabhushi, "Artificial intelligence in digital pathology—new tools for diagnosis and precision oncology," *Nat Rev Clin Oncol*, vol. 16, no. 11, pp. 703–715, 2019.
- [31] Y. Pan, B. Mirheidari, M. Reuber, A. Venneri, D. Blackburn, and H. Christensen, "Automatic hierarchical attention neural network for detecting AD," in *Proceedings of Interspeech 2019*, 2019, pp. 4105–4109.
- [32] P. Malhotra, L. Vig, G. Shroff, P. Agarwal, and others, "Long Short Term Memory Networks for Anomaly Detection in Time Series.," in *Esann*, 2015, p. 89.
- [33] Y. Zhang, X. He, Y. H. Chan, Q. Teng, and J. C. Rajapakse, "Multi-modal graph neural network for early diagnosis of Alzheimer's disease from sMRI and PET scans," *Comput Biol Med*, vol. 164, p. 107328, 2023.
- [34] M. G. Alsubaie, S. Luo, and K. Shaikat, "Alzheimer's Disease Detection Using Deep Learning on Neuroimaging: A Systematic Review," *Mach Learn Knowl Extr*, vol. 6, no. 1, pp. 464–505, 2024.
- [35] X. Xu, L. Lin, S. Sun, and S. Wu, "A review of the application of three-dimensional convolutional neural networks for the diagnosis of Alzheimer's disease using neuroimaging," *Rev Neurosci*, vol. 34, no. 6, pp. 649–670, 2023.
- [36] F. Lateef, M. Kas, and Y. Ruichek, "Saliency heat-map as visual attention for autonomous driving using generative adversarial network (gan)," *IEEE Transactions on Intelligent Transportation Systems*, vol. 23, no. 6, pp. 5360–5373, 2021.
- [37] M. Odusami, R. Maskeliūnas, and R. Damaševičius, "Optimized Convolutional Fusion for Multimodal Neuroimaging in Alzheimer's Disease Diagnosis: Enhancing Data Integration and Feature Extraction," *J Pers Med*, vol. 13, no. 10, p. 1496, 2023.
- [38] D. Agarwal, G. Marques, I. de la Torre-Díez, M. A. Franco Martin, B. García Zapira, and F. Martín Rodríguez, "Transfer learning for Alzheimer's disease through neuroimaging biomarkers: a systematic review," *Sensors*, vol. 21, no. 21, p. 7259, 2021.
- [39] Y. Zhu, X. Liang, J. A. Batsis, and R. M. Roth, "Exploring deep transfer learning techniques for Alzheimer's dementia detection," *Front Comput Sci*, vol. 3, p. 624683, 2021.
- [40] G. Devi, "A how-to guide for a precision medicine approach to the diagnosis and treatment of Alzheimer's disease," *Front Aging Neurosci*, vol. 15, p. 1213968, 2023.
- [41] B. Y. Kasula, "A Machine Learning Approach for Differential Diagnosis and Prognostic Prediction in Alzheimer's Disease," *International Journal of Sustainable Development in Computing Science*, vol. 5, no. 4, pp. 1–8, 2023.
- [42] A. G. Vrahatis, K. Skolariki, M. G. Krokidis, K. Lazaros, T. P. Exarchos, and P. Vlamos, "Revolutionizing the early detection of Alzheimer's disease through non-invasive biomarkers: the role of artificial intelligence and deep learning," *Sensors*, vol. 23, no. 9, p. 4184, 2023.
- [43] A. A. A. El-Latif, S. A. Chelloug, M. Alabdulhafith, and M. Hammad, "Accurate detection of Alzheimer's disease using lightweight deep learning model on MRI data," *Diagnostics*, vol. 13, no. 7, p. 1216, 2023.
- [44] Y. Xu, S. Hou, X. Wang, D. Li, and L. Lu, "A medical image segmentation method based on improved UNet 3+ network," *Diagnostics*, vol. 13, no. 3, p. 576, 2023.
- [45] A. W. Salehi et al., "A study of CNN and transfer learning in medical imaging: Advantages, challenges, future scope," *Sustainability*, vol. 15, no. 7, p. 5930, 2023.
- [46] N. N. Prakash, V. Rajesh, D. L. Namakhwa, S. D. Pande, and S. H. Ahammad, "A DenseNet CNN-based liver lesion prediction and classification for future medical diagnosis," *Sci Afr*, vol. 20, p. e01629, 2023.
- [47] A. Rayan et al., "Utilizing CNN-LSTM techniques for the enhancement of medical systems," *Alexandria Engineering Journal*, vol. 72, pp. 323–338, 2023.
- [48] M. M. S. Fareed et al., "ADD-Net: an effective deep learning model for early detection of Alzheimer disease in MRI scans," *IEEE Access*, vol. 10, pp. 96930–96951, 2022.
- [49] S. Mahmood et al., "A Robust Deep Model for Classification of Peptic Ulcer and Other Digestive Tract Disorders Using Endoscopic Images," *Biomedicines*, vol. 10, no. 9, p. 2195, 2022.
- [50] T. M. Ghazal et al., "Alzheimer Disease Detection Empowered with Transfer Learning.," *Computers, Materials & Continua*, vol. 70, no. 3, 2022.
- [51] G. Ahmed et al., "Dad-net: Classification of alzheimer's disease using adasyn oversampling technique and optimized neural network," *Molecules*, vol. 27, no. 20, p. 7085, 2022.
- [52] G. Ahmed, M. J. Er, S. Zikria, and M. S. Fareed, "Detection of Alzheimer's Disease using Deep Learning: An Optimized Approach," in *2023 6th International Conference on Intelligent Autonomous Systems (ICoIAS)*, 2023, pp. 148–155.