Deep Learning Approaches for Early Detection of Alzheimer's Disease using MRI Neuroimaging

M S Bhargavi
Department of Computer Science and Engineering
Bangalore Institute of Technology
Bengaluru, India
ORCID: 0000-0002-6576-6555

Bharani Prabhakar
Department of Computer Science and Engineering,
Bangalore Institute of Technology
Bengaluru, India
bharaniprabhakar22@gmail.com

Abstract*—Alzheimer's disease is a neurodegenerative disorder and one of the most prevalent forms of progressive Dementia. Alzheimer's disease does not have any cure as it leads to brain shrinkage and damage of the brain cells. Early detection can aid in assessing and administering suitable treatment that can slow down disease progression. Progressive monitoring of individuals diagnosed with Mild Cognitive Impairment (MCI) through neuroimaging has gained considerable interest recently for early detection. The most popular neuroimaging used being the Magnetic Resonance Imaging (MRI). The intention of monitoring individuals diagnosed with MCI is that, MCI diagnosed are more likely to get converted to Alzheimer's. Deep learning models have proven to be very effective and shown powerful performance in neuroimaging analytics. Deep learning techniques have been employed over brain MRI for assessing Alzheimer's disease progression and gained immense popularity in recent times due to its commendable performance. In this paper, we present a study on the applications of Deep learning techniques in early detection and progression of Alzheimer's disease. The study focuses on recent advances in the early detection of Alzheimer's using Deep learning models and MRI neuroimaging.

***Keywords*— Alzheimer's Disease, Neuroimaging, Magnetic Resonance Imaging, Deep Learning, Mild Cognitive Impairment**

I. Introduction

Alzheimer's disease (AD) is a neurological disorder that affects the brain and makes people demented and forgetful [1]. Alzheimer's disease is majorly seen among elderly population over the age of 60 years. People with early Alzheimer's find performing activities such as maintaining accounts very difficult. Other common problems include wandering and getting lost. In the moderate stage of the disease, patient tends to develop confusion and in some cases there is loss of primary senses of smell and taste. Recognition of family and friends becomes a problem. Alzheimer's patients are generally very aggressive. Small issues tend to bother them. They start having hallucinations, delusions and paranoia. In the last stage or the severe stage, the patient usually becomes bedridden and completely depends on another person for basic activities [2].

Over 50 million people worldwide are diagnosed with dementia, out of which, two-thirds of them have Alzheimer's disease. There is at least one new case of Alzheimer's diagnosed every three seconds worldwide [3]. There is no treatment or cure for the disease. Proper care and medication helps in delaying the severity of the disease. Early and effective diagnosis plays an important role in starting early medication and care to improve the lifestyle of the patients. There is a need for development of innovative methods for early diagnosis and support the battle against Alzheimer's disease. Early detection would aid in administering preventive medical treatments and measures in the initial phase itself that can avoid further damage to the brain cells.

To develop effective diagnosis, understanding Alzheimer's progression is essential. The disease brings about functional as well as structural changes in the brain. Initially, patient develops Mild Cognitive Impairment (MCI) which is an intermediate phase and may gradually progress to AD [4]. A person with MCI is more prone to develop AD than the one not diagnosed with MCI. For early diagnosis of the disease, the main emphasis in research must be to predict the progression of MCI to AD. All MCI diagnosed individuals will not progress to Alzheimer's. The variations in the brain causing this conversion can be effectively measured using neuroimaging [5]. The most common and effective among the neuroimaging techniques used for AD prediction is the MRI of the brain [6].

Several studies have taken place using deep learning models for detection of AD versus Healthy Controls (HC) from MRI of the brain. Deep learning models have shown praiseworthy performance in image analytics over machine learning models. In recent times, this has contributed to intensification of research in early detection of AD using deep learning and brain MR imaging which require progressive monitoring from MCI to AD. The automated learning of features corresponding to the regions of interests in neuroimages and eliminating the need for annotations have provided immense popularity to deep learning models. This learning aids in localizing brain abnormalities, classification of brain disorders and predicting disease progression. Many novel approaches have been proposed by researchers. A better understanding of various applications of deep learning over brain MRI to develop more robust and efficient techniques is required. Hence, in this paper, we present a study on recent advances in the early detection of Alzheimer's disease using deep learning on brain MR imaging. Considerable progress in research in this arena has taken place in the last five years only and hence this study focusses on work post 2017 as prior to that the focus of all research work was only effective detection of AD using MRI with deep learning and not early detection. Only refereed journal articles are considered for this study.

The rest of the paper is structured as follows: Section II discusses the open source databases used in Alzheimer's studies. Section III demonstrates the types of neuroimaging techniques and the various classifications under AD. Section IV summarizes the research works that have employed deep learning on MRI for early Alzheimer's detection. Section V concludes the paper.

II. DATASETS FOR ALZHIEMER'S DISEASE DETECTION

Research in Alzheimer's prediction has progressed to a larger extent due to the availability of open source databases. This section discusses the most widely used open source databases for the study of Alzheimer's disease and for the development of effective predictive models.

Alzheimer's Disease Neuroimaging Initiative (ADNI) [7]: The dataset used by majority of the research works considered in this study is ADNI open source dataset. ADNI database was released in 2003 headed by Michael W. Weiner, Principal Investigator. ADNI has reliable clinical data and images that can be utilized for developing models for prediction of AD. The database consists of series of MRI images, Positron Emission Tomography (PET) images, cognitive tests, genetics, cerebrospinal fluid (CSF) and blood biomarkers for developing prediction models.

Open Access Series of Imaging Studies (OASIS) [8]: OASIS has made neuroimaging and processed image datasets of normal aging and AD freely available to scientific community. It has been generated by Knight Alzheimer Disease Research Center and hosted by central.xnat.org. The recent release is version OASIS 3.

Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing (AIBL) [9]: AIBL was instituted in 2006 and the focus is on large cohort studies of patients enrolled as AD, MCI and Healthy. The database consists of Image data: MRI and PET, clinical data, cognitive data, biomarkers such as blood, genotype, ApoE and others.

III. NEUROIMAGING TECHNIQUES AND CLASSIFICATIONS OF ALZHEIMER'S DISEASE

This study is based on Neuroimaging data. Neuroimaging data is very complex as it encompasses various features related to the size, pathology, structure and functionality of the brain. Neuroimaging, also called as brain imaging is done using various techniques. Different techniques are Magnetic Resonance Imaging (MRI), Computerized Tomography (CT), Magnetoencephalography (MEG), Positron Emission Tomography (PET), functional near-infrared spectroscopy (fNIRS) and Electroencephalography (EEG) [10]. Most commonly used for Alzheimer's analysis is MRI. Under MRI neuroimaging, functional MRI (fMRI) and structural MRI (sMRI) are widely used for AD prediction. sMRI is used to determine the anatomical structure of the brain and fMRI determines the metabolic function of the brain [11].

Researchers have utilized sMRI / fMRI to perform image feature extraction and classifications pertaining to AD. The classifications are between: (i) AD and Healthy Controls (HC) / Cognitively Normal (CN), (ii) MCI and HC, (iii) MCI-converter (MCI-c) / MCI-progressive (MCI-p) - MCI Patients who will progress to AD and MCI non-converter (MCI-nc) / MCI stable (MCI-s) - MCI patients who won't progress to AD. For early detection of AD, MCI-c versus MCI-nc and MCI-c versus AD classification is of utmost importance. As the disease progression is gradual from MCI diagnosed individuals, it is very difficult at baseline to classify patients as progressive MCI. Deep learning approaches have shown encouraging results in detecting this progression.

IV. DEEP LEARNING APPROACHES FOR EARLY DETECTION OF ALZHIEMER'S DISEASE USING MRI

Remarkable performance of deep learning models in image analytics has inspired researchers in the application of deep learning to neuroimaging data. Recently, many research works have been published using deep learning models on variants of MRI neuroimaging for early detection of Alzheimer's. This section discusses recent progress made by researchers in early detection of AD using deep learning and brain MRI. Factors that are reflected from each research work are: the type of MR image considered, feature extraction process, classifications of disease progression, accuracy scores of classifications, deep learning approach and dataset used.

Wee et al. [12] employed Convolutional Neural Network (CNN) based on spectral graph. Along with the input, output and full connected layers, the graph variant deep learning model has 3 graph convolutional layers. The deep learning model incorporates cortical thickness in order to recognize MCI progression to AD with T1 weighted brain MRIs. The images are acquired from ADNI – 1083 subjects from ADNI-2 and 1012 subjects from ADNI-1. Images are also inclusive of 347 Asian subjects. The spectral graph CNN achieved an accuracy of 74% in progression prediction from early MCI to AD and 92% on Late MCI to AD.

Hongming Li et al. [13] propose a deep learning method based on structural MRI. Deep learning extracts relevant features from hippocampal MRI and these extracted features are further used to predict disease progression. Features learnt by the deep learning model are utilized to predict the progression time of individual to AD using LASSO regularized Cox regression model. They included data from ADNI (1711 subjects) and AIBL (435 subjects) for their experimentations. To evaluate accuracy of disease progression, concordance index (C-index) was used and the model obtained C-index of 0.762 using hippocampal features which is better than studies performed using shape and texture image features.

Simeon Spasov et al. [14] presents a deep learning model that has a layer for 3D separable convolutions. Structural MRI is used along with demographic, neuropsychological and genetic data contributing to dual learning. To reduce data overfitting, fewer parameters are employed in the neural network classifier compared to other deep learning architectures. The image data is acquired from ADNI (785 subjects). The model identified MCI patients who are likely to develop AD in the next 3 years with an accuracy of 86%.

Silvia Basaia et al. [15] use structural MRI scans for the experimentations that are single, cross-sectional. CNN is employed on three dimensional T1 weighted images to predict individuals who have been diagnosed with MCI to convert to AD or MCI-c. Images have been used from ADNI and some participants were recruited at their institute for the study. The performance accuracy of CNN was tested in distinguishing HC, AD, MCI-c and MCI-s. Highest accuracy was achieved in classifications between AD and HC. However, 75% accuracy was achieved in discriminating between patients with MCI-c and MCI-s using CNN.

Mingxia Liu et al [16] developed neural network model which is densely connected for AD progression assessment. They use MRI and clinical data from baseline to multiple time points for progression prediction and term this as weakly supervised. Preprocessing of MRI scans is performed to extract multi-scale image patches and capture structural information of images. A joint prediction is performed using CNN to estimate scores at multiple time points. MRI and clinical data used in this model is from ADNI. The experiment is performed on 1469 subjects from the ADNI database. It was seen that the model could successfully predict progressive scorings at future time-points.

Anees Abrol et al. [17] proposed modified deep residual neural network (ResNet) model. Initially the deep model was trained using MCI diagnosed subjects only. Post this, a transfer learning was trained on AD and HC. The proposed framework could capture non-linear features for successful prediction of AD progression. Resnet could extract low dimensional features from smoothed three dimensional images. This improved classification accuracy and also was able to identify regions that affected the progression from MCI to AD. The data was acquired from ADNI and a total of 828 subjects were studied falling in different categories: CN, stable MCI, progressive MCI and AD. They have achieved an accuracy of 88.1% for stable MCI versus AD and 77.8% for stable MCI versus progressive MCI.

Dan Pan et al. [18] have proposed an approach to combine Convolutional Neural Network and ensemble learning. Sagittal, transverse and coronal slices of MRI were used to train a number of CNN models. The trained CNNs were fused together into an ensemble. Based on the slices and highest discriminating points leading to best classification, brain regions contributing to early diagnosis were identified. The data for the study was acquired from ADNI: 787 subjects falling into categories HC, MCI-c, MCI-nc and AD. 79% accuracy is obtained for HC versus MCI-c and 69% for MCI-c versus MCI-nc.

Fei Gao et al. [19] propose an Age-adjust neural network which employs transfer learning in two phases: In phase-1, a feature extraction and age prediction is done using pre-trained network. In phase-2, the knowledge of predictions and the features of phase-1 is transferred for MCI-c prediction. This transfer learning approach addresses the limited availability of medical neuroimaging data. Experimentations are conducted on T1 weighted MR images of 1144 subjects obtained from ADNI and Information eXtraction from Images (IXI) [20] database falling into categories MCI-c and MCI-nc. 81% accuracy was achieved using this model.

Atif Mehmood et al. [21] propose transfer learning and tissue segmentation of MRIs to extract the gray matter tissue for early detection of AD. This approach overcomes the requirement of large annotated datasets for training. In transfer learning, VGG architecture is used with pre-trained weights. The study is performed using dataset from ADNI of 300 subjects with categories: NC, late MCI, early MCI and AD. The accuracy obtained for early MCI versus AD is 83.69%.

Jinhyeong Bae et al. [22] proposes a deep learning model to address Dementia Alzheimer's type development. Structural MRI served as input for three dimensional Convolutional neural network. The three dimensional CNN is trained using transfer learning and HC scans and Dementia Alzheimer's type scans were used to pre-train the model. Data was acquired from ADNI of 1530 subjects with categories of HC, MCI convertible, MCI non-convertible scans. The model shows 82.4% accuracy on target classes – MCI-c and MCI-nc.

A DEMentia NETwork (DEMNET) was proposed by Suriya Murugan et al. [23], for identifying four different stages of Dementia. A new CNN architecture with lesser number of parameters has been suggested. The class disproportion problem is overcome using Synthetic Minority Oversampling Technique popularly termed SMOTE analysis. They experimented with datasets from Kaggle consisting of 6400 MR images and classified the images into 4 dementia classes – Mild, Moderate, Severe and No Dementia. They also did a 5-way classification on 1296 images of ADNI: AD, MCI, EMCI, LMCI and HC. They achieved an accuracy of

95.23% and 85% with and without SMOTE respectively.

TABLE I. OVERVIEW OF RECENT RESEARCH USING DEEP LEARNING MODELS AND MRI FOR EARLY DETECTION OF AD

Authors (Year)	Classifications	Overall Sample Size	Database	Modality	Deep Learning Model
Jun Shi et al. (2017)	AD vs HC, MCI vs HC, MCI-c vs MCI-nc, AD vs MCI-c vs MCI-nc vs. HC	301 subjects	ADNI	MRI + PET	Multimodal Stacked Deep Polynomial Network
Wee et al. (2019)	HC vs AD, HC vs LMCI, HC vs EMCI, EMCI vs LMCI, EMCI vs AD, LMCI vs AD	2095 (ADNI subjects) & 347 (Asian subjects) ADNI-1 3602+ ADNI-2 3187 images	ADNI	T1-weighted MRI	Spectral Graph CNN
Hongming Li et al. (2019)	HC vs AD MCI vs AD	1711-ADNI subjects, 435-AIBL subjects	ADNI & AIBL	Hippocampal sMRI + Clinical Data	CNN
Simeon Spasov et al. (2019)	HC vs AD MCI vs AD	785 subjects	ADNI	sMRI + Demographic + Neuropsychological +APOe4 Genetic Data	3D-CNN
Silvia Basaia et al. (2019)	HC vs AD, c-MCI vs HC, s-MCI vs HC, AD vs c-MCI, AD vs s-MCI, c-MCI vs s-MCI	1409 ADNI subjects, 229 Milan subjects	ADNI & Milan Dataset	3D T1-weighted MRI	3D-CNN
Garam Lee et al. (2019)	MCI-c vs MCI-nc	1618 subjects	ADNI	MRI+ Demographic Information+ Cognitive Performance + CSF	Multimodal Recurrent Neural Network
Mingxia Liu et al. (2020)	AD vs p-MCI vs s-MCI vs HC	1469 subjects	ADNI	T1-weighted MRI + Clinical Data	CNN
Anees Abrol et al. (2020)	HC vs AD, HC vs p-MCI, s-MCI vs AD, s-MCI vs p-MCI, HC vs s-MCI, p-MCI vs AD	828 subjects	ADNI	sMRI	Modified Deep ResNet
Dan Pan et al. (2020)	HC vs AD MCI-c vs HC, MCI-c vs MCI-nc	787 subjects	ADNI	Sagittal, Coronal, or Transverse MRI slices	CNN with Ensemble Learning
Fei Gao et al. (2020)	MCI-c and MCI-nc	847 (ADNI & IXI subjects) 297 ADNI subjects	ADNI & IXI	sMRI + Age	Age-adjust Neural Network – Transfer Learning
Atif Mehmood et al. (2021)	HC vs AD, HC vs EMCI, HC vs LMCI, EMCI vs LMCI, EMCI vs AD, LMCI vs AD	300 subjects	ADNI	GM scans from T1-weighted MRI	CNN – Layerwise Transfer Learning with VGG-19
Jinhyeong Bae et al. (2021)	MCI-c vs MCI-nc	1530 subjects 3490 images	ADNI	sMRI	3D-CNN-Transfer Learning with a base model of ResNet29
Suriya Murugan et al. (2021)	MID vs MOD vs ND vs VMD AD vs MCI vs EMCI vs LMCI vs HC	6400 images (Kaggle) & 1296 images (ADNI)	ADNI & Kaggle Dataset	MRI	2D-CNN - DEMNET
Hadeer A. Helaly et al. (2021)	AD vs EMCI vs LMCI vs HC	300 subjects 21816 images	ADNI	T1-weighted MRI	CNN – Transfer Learning with VGG-19
Ahed Abugabah et al. (2022)	HC vs AD, MCI vs AD, HC vs MCI	375 subjects	ADNI	WM, GM, CSF from MRI	DCNN
Modupe Odusami et al. (2022)	AD vs MCI vs EMCI vs LMCI vs HC	7509 images	ADNI	MRI	ResNet18 and DenseNet201

Abbreviations: LMCI – Late MCI, EMCI – Early MCI, sMRI – Structural MRI, c-MCI – Convertible MCI, s-MCI – Stable MCI, p-MCI – Progressive MCI, MCI-c – MCI converter, MCI-nc – MCI non-converter, MID- Mild Demented, MOD – Moderate Demented, ND – Non-Demented, VMD – Very Mild Demented, WM – White Matter, GM – Grey Matter

Hadeer A. Helaly et al. [24] presents two different techniques for early predictions of AD. In one, they use a convolutional neural network architecture for classifying 2D and 3D structural MRI into 4 different classes of AD. In another, transfer learning is employed using pre-trained VGG19 model. T1 weighted MRI images are acquired from ADNI of 300 subjects with categories: HC, AD, early MCI, late MCI. CNN obtained a multi-class classification accuracy of 93.61% and 95.17% for 2D and 3D. With VGG, an accuracy of 97% is obtained.

Ahed Abugabah et al. [25] proposed a model based on deep CNN. Grey matter, white matter tissues of MR imaging and cerebrospinal fluid is used to build the model. They experimented on datasets from ADNI with 375 subjects including categories: AD, MCI and HC. They achieved an accuracy of 92.84% for MCI versus AD.

Modupe Odusami et al. [26] develop ResNet18 and DenseNet121 deep CNN architecture that automatically extracts randomized deep features from brain functional networks in MR images. The concatenated deep features are further used for 3-way, 4-way and 5-way classifications of MR images with an accuracy of 98.21%, 93.06% and 98.86% respectively. The five categories are AD, early MCI, late MCI, MCI, CN. 7509 images are obtained from ADNI.

Jun Shi et al. [27] fuses multi-modal neuroimaging data: PET and MRI for early detection of AD. A deep polynomial networks is proposed to amalgamate PET and MRI multi-modality and learn feature representation in a stacked manner. Two stacked deep polynomial networks are used: one to learn features from PET and MRI, another to fuse the learnt features. Same number of PET and MRI images are acquired from ADNI of 301 subjects categorized as AD, HC, MCI-c and MCI-nc. The classification accuracy for MCI-c versus MCI-nc is 76.52±5.99 %. For a 4-way classification involving HC, AD, MCI-c and MCI-nc, the accuracy is 57.00±3.65%.

Garam Lee et al. [28] proposed multi-modal Recurrent Neural Network (RNN) for MCI versus AD prediction. The framework fuses at baseline, three multi-modal biomarkers: neuroimaging, cerebrospinal fluid and biomarkers of cognitive performance. The multi-modal data is obtained from ADNI. 1618 subjects were considered with categories: CN, MCI-c, MCI-nc, AD. The results showed that MCI conversion to Alzheimer's accuracy was 75% using single modality and the prediction model showed 81% accuracy while incorporating longitudinal multi modal data.

Research works on early detection of AD using MRI as primary modality and employing deep learning models are summarized in Table I. Table I summarizes work post 2017 and only works from refereed journals are considered.

V. CONCLUSION

In this paper, we studied recent research works where deep learning on MR imaging were used for early detection and prognosis of AD from MCI. Deep learning models such as 2D CNN, 3D CNN, Stacked auto encoders, variants of ResNet, DenseNet, VGG, Deep Polynomial Networks, RNN have been employed for early detection of AD. A lot of research using deep learning and MRI for detection of HC versus AD has taken place obtaining very high accuracies. However, as per the study, the classification accuracy scores for MCI versus AD for early detection using deep learning has always been lower when compared to HC versus AD. This is because progressive MCI would possess similar traits to AD when compared to HC and discrimination would require robust deep learning models. Multi-modality can improve the detection accuracies. Very few papers are available on multi-modality with deep learning for early detection of AD. This could be because deep learning extracts relevant features automatically from input images without any form of preprocessing and feature selection. This can result in difficulty integrating other clinical data such as PET, CSF and blood biomarkers, genetics or cognitive tests. However, multi-modal learning ensures incorporating different perspectives and improve diagnostic classification accuracies and must be explored to a larger extent.

REFERENCES

[1] Dementia Statistics – Alzheimer's Disease International. url: https://www.alz.co.uk/research/stastics

[2] Reisa A S , Paul S A, Laurel A B, David A B, Suzanne C, Anne M F, Takeshi I, Clifford R J Jr, Jeffrey K, Thomas J M, Denise C P, Eric M R, Christopher C R, Eric S, Yaakov S, Kristine Y, Maria C C, Bill , Marcelle M B, Molly V W and Creighton H P, "Toward defining the preclinical stages of Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease." Alzheimer's & dementia : the journal of the Alzheimer's Association vol. 7,3, pp 280-92, 2011.

[3] Sandra M, Hrvoje B, Valbona G and Vida D "Possibilities of Dementia Prevention - It is Never Too Early to Start." Journal of medicine and life vol. 12,4, pp 332-33, 2019.

[4] Kevin G, Michael O , Oisin H, Irene B, Mathew G, Robert C, Elaine G, Brian A L, David R, "Clinical utility of mild cognitive impairment subtypes and number of impaired cognitive domains at predicting progression to dementia: A 20-year retrospective study." International Journal of Geriatric Psychiatry vol,36.1, pp 31-37, 2021.

[5] Jack de la Torre "The vascular hypothesis of Alzheimer's disease: a key to preclinical prediction of dementia using neuroimaging." Journal of Alzheimer's Disease vol. 63.1, pp 35-52, 2018.

[6] Jo, Taeho, Kwangsik Nho, and Andrew J. Saykin. "Deep learning in Alzheimer's disease: diagnostic classification and prognostic prediction using neuroimaging data." Frontiers in aging neuroscience, vol.11, p 220, 2019.

[7] Alzheimer's Disease Neuroimaging Initiative (ADNI) url: https://adni.loni.usc.edu/data-samples/access-data/

[8] Open Access Series of Imaging Studies (OASIS) url: https://www.oasis-brains.org/

[9] Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing (AIBL) url: https://aibl.csiro.au/

[10] Lai, Chien-Han. "Promising neuroimaging biomarkers in depression." Psychiatry Investigation, vol. 16.9, p 662, 2019.

[11] Prajapati Rutvi and Isaac Arnold Emerson. "Global And Regional Connectivity Analysis of Resting-State Function MRI Brain Images Using Graph Theory in Parkinson's Disease" International Journal of Neuroscience, vol. 131.2, pp 105-115, 2021.

[12] Chong-Y W, Chaoqiang L, Annie L, Anqi Q, "Cortical graph neural network for AD and MCI diagnosis and transfer learning across populations." NeuroImage. Clinical vol. 23, p 101929, 2019.

[13] Hongming L, Mohamad H, David A W and Yong F, "A deep learning model for early prediction of Alzheimer's disease dementia based on hippocampal magnetic resonance imaging data." Alzheimer's & dementia : the journal of the Alzheimer's Association vol. 15,8, 2019, pp 1059-1070.

[14] Spasov S, Passamonti L, Duggento A, Liò P, Toschi N, "A parameter-efficient deep learning approach to predict conversion from mild cognitive impairment to Alzheimer's disease" Neuroimage, vol.189, pp 276–87, 2019.

[15] Silvia Basaia, Federica Agosta, Luca Wagner, Elisa Canu, Giuseppe Magnani and Roberto Santangelo, Massimo Filippi, “Automated classification of Alzheimer's disease and mild cognitive impairment using a single MRI and deep neural networks.” NeuroImage. Clinical vol. 21, p 101645, 2019.

[16] Mingxia L, Jun Z, Chunfeng L, and Dinggang S, “Weakly supervised deep learning for brain disease prognosis using mri and incomplete clinical scores.” IEEE transactions on cybernetics vol. 50,7, pp 3381-3392, 2020.

[17] Anees A, Manish B, Alex F, Yuhui D, Sergey P and Vince C “Deep residual learning for neuroimaging: An application to predict progression to Alzheimer's disease.” Journal of neuroscience methods vol. 339, p 108701, 2020.

[18] Dan P, An Z, Longfei J, Yin H, Tory F, Xiaowei S, “Early detection of alzheimer's disease using magnetic resonance imaging: a novel approach combining convolutional neural networks and ensemble learning.” Frontiers in neuroscience vol. 14, p 259. 13 May. 2020.

[19] Gao Fei,Yoon Hyunsoo, Xu Yanzhe, Goradia Dhruman, Luo Ji, Wu Teresa and Su Yi, “AD-NET: Age-adjust neural network for improved MCI to AD conversion prediction.” NeuroImage. Clinical vol. 27, p 102290, 2020.

[20] Information eXtraction from Images (IXI), url: https://brain-development.org/ixi-dataset/

[21] Atif M, Shuyuan Y, Zhixi F, Min W, Al S A 1, Rizwan K, Muazzam M, Muhammad Y, “A transfer learning approach for early diagnosis of alzheimer's disease on mri images.” Neuroscience, vol. 460, pp 43-52, 2021.

[22] Bae J, Stocks J, Heywood A, Jung Y, Jenkins L, Hill V, “Transfer learning for predicting conversion from mild cognitive impairment to dementia of Alzheimer’s type based on a three-dimensional convolutional neural network.” Neurobiol Aging. vol. 99, pp 53–64, 2021.

[23] Suriya, M, Chandran, V, M G, Sumithra, Gao, Xiao-Zhi, Elakkiya, B, Akila, M Subramanian and Dr. Manoharan “DEMNET: A Deep Learning Model for Early Diagnosis of Alzheimer Diseases and Dementia from MR Images” IEEE Access, vol.9, pp 90319-90329, 2021.

[24] Hadeer A. H, Mahmoud B & Amira Y H "Deep Learning Approach for Early Detection of Alzheimer’s Disease." Cognitive Computation, pp 1-17, 2021.

[25] Ahed A, Atif M, Sultan A and Ahmad A. L. S "Health care intelligent system: a neural network based method for early diagnosis of alzheimer's disease using mri images." Expert Systems, 2022.

[26] Modupe Odusami, Maskeliūnas Rytis, and Robertas Damaševičius. "An intelligent system for early recognition of alzheimer’s disease using neuroimaging." Sensors, vol. 22.3, p 740, 2022.

[27] Jun S, Xiao Z, Yan L, Qi Z, Shihui Y, "Multimodal neuroimaging feature learning with multimodal stacked deep polynomial networks for diagnosis of Alzheimer's disease." IEEE journal of biomedical and health informatics, vol. 22.1, pp. 173-183, 2017.

[28] Lee G, Nho K, Kang B, Sohn KA, Kim D, Weiner MW, “ Predicting Alzheimer’s disease progression using multi-modal deep learning approach” Sci Rep, vol 9(1), 2019.