IOP Conference Series: Materials Science and Engineering

PAPER • **OPEN ACCESS**

Deep Learning Based Multilevel Classification of Alzheimer's Disease using MRI Scans

Deep Learning Based Multilevel Classification of Alzheimer's Disease using MRI Scans

Manu Raju[1], Thirupalani M[2], Vidhyabharathi S[3] and Thilagavathi S[4]

1 Assistant Professor, Bannari Amman Institute of Technology, Department of Electronics and Communication Engineering, Erode, Tamilnadu, India.
2,3,4 Bachelor of Engineering, Bannari Amman Institute of Technology, Department of Electronics and Communication Engineering, Erode, Tamilnadu, India.

manuraju@bitsathy.ac.in, thirupalani.ec18@bitsathy.ac.in, vidhyabharathi.ec18@bitsathy.ac.in, thilagavathi.ec18@bitsathy.ac.in

Abstract. Alzheimer's disease is one of the most frequently studied diseases of the nervous system although it has no cure or slowing its progression. There are various options for treating the symptoms of Alzheimer's disease in different stages and as the disease progresses over time, patients in their various stages need different treatment. Diagnosis of Alzheimer's in the elderly is quietly difficult and requires representation of a discriminatory factor in isolation due to similar brain patterns and pixel strength. Deep learning strategies are able to learn such representations from the data. In this proposed work we perform multilevel classification of Alzheimer's disease ie; Mild Demented, Moderate Demented, Non Demented and Very Mild Demented using transfer learning with VGG16 using Fastai. This approach results in 99% predictive accuracy which means a significant increase in accuracy compared to previous studies and clearly demonstrates the effectiveness of the proposed methods.

Keywords: Alzheimer's disease; MRI; Transfer Learning; VGG16; GradCam

1. Introduction

Alzheimer's Disease(AD) is a neurological, chronic and progressive brain disorder that leads to memory loss, less thinking ability and unable to perform simple tasks [1] . According to the statistics [2], the annual number of new cases of the Alzheimer's disease is anticipated to double by 2050. Therefore, it is very critical to diagnose the individuals with Alzhiemer's at an early stage. This will help to determine its progression and try various clinical treatments and improve the quality of life of a patient. Alzhiemer's disease results in the reduction of hippocampus region of the brain which is much more than the normal individual and also result in cerebral cortex reduction and the enlargement of ventricles of the brain. These regions perform functions including memory, planning, thinking, and judgment [3]. The stages of disease progression determines the amplitude of changes in different areas of the brain. Magnetic Resonance Imaging(MRI) can be used as a biomarker to indicate the volume reduction of hippocampal region and cerebral cortex and enlargement of ventricles [4].The coronal view of the brain MRI is shown in figure 1

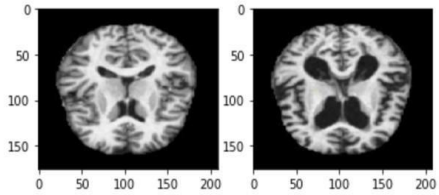

Figure 1: MRI Images from the Dataset of the Brain.

As there exist only small changes between Mild Cognitive Impairment (MCI), Alzhiemer's disease(AD) and Normal control (CN) it has become one of the most challenges for the doctors to understand them. Various clinical methodologies is been used by physicians to perform classification of alzhiemer's disease. Cerbrospinal fluid is a early indicator of alzhiemers disease , due to the deposition of neurofibrallary tangles and amyloid beta protien at the starting stage of disease. CSF is collected in a noninvasive manner, that is a puncture is made in the skull to collect the fluid from the brain ventricles. This procedure is tedious and dangerous as it may cause bleeding in the brain[5]. To overcome such problems medical imaging technologies can be used, in which neuroimaging techniques like Structural Magnetic resonance Imaging (SMRI) [6], Functional Magnetic Resonance Imaging(fMRI), FDG-Positron Emission Tomography(PET) [7] and Computer Tomography(CT) etc plays a vital role in determining the anatomical and functional changes in the brain. SMRI is the best biomarker to analyze structural changes caused by Alzheimer's disease [8].

Recent research in computer vision and machine learning has encouraged neural networks and indepth learning. Deep learning [9] is a representative learning method that allows the machine to read different representations from raw data the reason for making it popular with a high-quality and validated network structure. The main purpose of this research is to use deep learning strategies in the Kaggle database to differentiate the different stages of Alzheimer's disease. Moreover, the sub-objective of this research work is to identify the most distinguishing attribute for each of the different stages of the Alzheimer's disease among Kaggle dataset. The task is to improve the accuracy from 90% to 98-99%. Densenet161 gives 90% accuracy. The task is to optimize for accuracy but we will also show the F1 score of the model as well. This task will feature a vgg16 model, trained in FastAI, and using progressive resizing and cutout to attain better results.

2 . Literature survey

As early, researchers were using a variety of machine based methods to diagnose Alzheimer's disease from MRI data only. Investigators began by developing biomarkers that would be tested. Biomarker is an invaluable indicator of biological status. Hippocampal region has been used as an important biomarker by the doctors and proven to give high accuracy in diagnosing the AD.But, the hippocampal volume is not enough to predict the progression of mild dementia (MCI) to Alzheimer's disease [10]. Other factors also contribute to the disease progression such as the cortical areas, cortical thickness etc. Given the features of space in MRI scans, study equipment and in-depth study methods are often ideal for combining those divisive features [11]. Deep learning is a part of machine learning that enables richer and robust representation of features. In [12] auto encoders is used to integrate features from PET and MRI scans and achieved 92% accuracy in the binary phase of Alzheimer's disease [13]. They suggested independent component analysis and structural modelling to be a promising tools to detect the atropy patterns in local regions of brain MRI. An additional proposed method was to capture sequential fragments from MRI scans because it was assumed that each piece covered important areas of cognitive processing. [14] used DenseNet and integrated methods to separate all 3D MRI scan, which led to a new state of the art in three categories (Alzheimer's versus small cognitive impairment compared to normal comprehension) 97% accuracy. A good development of phased accuracy is seen in the work [15] VGG16 structures trained in a series of MRI scans and obtained about 98% accuracy. Another experimental work performed by used the ADNI database for high unit-based system performance and new artistic results are available for multiclass disease classification, the proposed method results in an estimated 98.8% accuracy. Hon and Khan did the same job but used a clever way

of selecting the pieces there use an entropy-based approach to data selection rather than data intuition. They then applied the learning transfer to two structures: VGG16 and Inception V4 [16] and compared the performance of both structures. They were able to achieve 96.25% accuracy in the binary phase with the construction of Inception V4 on the OASIS database. This approach also helps us to expand our approach to predicting a complex system [17]

3. Methodology

Transfer Learning technique is employed in this paper to train a pretrained deep learning architecture which helps us to build a new architecture using our dataset without training from the scratch and thus avoid the need of huge dataset. The block diagram of the proposed method is given in figure 2. The two dimension MRI image slices of coronal view is downloaded from kaggle. The images is proprocessed by peforming intensity normalization and skull stripping. Further the image is fed into the VGG16 architecture working with Fastai for classification. In our work we go with four way classification i.e; Mild demented, Moderate demented,Very mild demented and Normal controls. Finally the brain affected region computed by algorithm for each classes is projected into MRI images using GradCam [18]. Our dataset is different from ImageNet so we have to retrieve fully connected layers trained with our classification task , whereas the weights of convolutional layers is not required for much modification. The convolutional layers found at the starting of architecture usually learn lower level features which will be common for all images and can be easily optimized [19]. But, the convolutional at the last stages will be trained for representations of high level features that require more optimization while training. In this paper we have trained with complete architecture and allowing all weights to change which helps to learn the subtle changes specific to our problem.

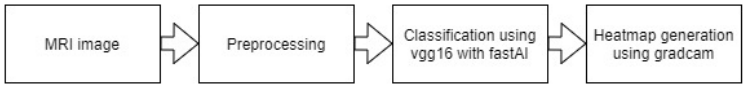

Figure 2: Block Diagram of proposed work.

Vgg16 is a standard convolutional neural network that consist of many layers of convolutional blocks with multiple integration within several layers and fully integrated at the end of the layer [20]. The last layer consist of same number of storage nodes as the number of division in classification task which use the softmaax function. The softmax function is defined as

$$\sigma(\vec{z})=\frac{e^{z_i}}{\sum_{j=1}^{k} e^{z_j}} \quad (1)$$

where σ is the softmax function, z is the input vector, k number of classes for multiclass classifier. The softmax function computes the conditional probability of each class given the input image. Similarly it gives the probability for all the classes. The model tries to come with the highest conditional probability of the particular class corresponding to the feature vector at the fully connected layer. The VGG16 network was modified by inserting a new untrained dense layer at the end of the network. We then trained the complete network using our training dataset. The cost function used is the categorical cross entropy for multiclass classification. The categorical-cross entropy is defined as

$$E(x,y)=\sum_{z\epsilon Z} X(z)\log(Y(z)) \quad (2)$$

Where X is the true and Y is the true and computed distribution respectively. We tried with an Adam optimizer which has the capability to optimize the moment adaptively. This optimizer has the following benefits it is computationally efficient, simple to implement, its hyper-parameters have intuitive interpretation and requires little tuning. Neverthless, the adam optimizer works good for data having non stationary characteristics and a non convex optimization problem, but our optimization problem is stationary and covex. So the function did not suit for our problem. After doing much emperical studies it is found that for medical imaging stochastic gradient descent with Nesterov intensity gives good performance. Nesterov's momentum helps to facilitate the movement of local territory that it may encounter on the way to the true weights. There is a improvement in performance when we moved from Adam to SGD with Nestrov and the best value chosen for momentum is 0.9.

3.1 Fastai

Fastai is a deep learning library that can be used to enhance the performance and speed up the operation of deep learning algorithms in minimum time [21]. It allows the beginners and practitioners to use pre existing deep learning models in high level API in a more productive manner. The default settings intelligently choosen based on pevious experience and practices help to achieve state of art in research. It also provides customizable lower level API which help to build function as per the requirement. Here we use VGG16 transfer learning to be performed using fastai which help us to optimise the batch normalization training, layer freezing etc.

3.2 Gradcam

Grad-CAM uses the gradient data that goes into the final decision-making layers to get a working class map [22]. We measure all channels by the last class gradient in relation to that channel. This "makes" different channels depending on how much those channels affect the output category

$$S^c = (1/K) \sum_i \sum_j \sum_k (\partial y^c / \partial A^j_{ik}) A^j_{ik} \quad (3)$$

S^c gives the global average pooling for the gradient of output label y^c with respect to the feature map A^j_{ik} over dimensions i and j. we multiply this by the channel to get the class activations. Unlike normal class activation maps, this does not require retraining the network as the class activation is determined before the flattening layer. By using GradCAM along with training multiple models, you can ensure that classifiers are predicting classes for the correct reasons without needing to retrain the network. We think this is especially important for detecting Alzheimer's - there could be many mislabels early with behavioral evaluations. Ensuring classifiers are identifying Alzheimer's through the correct brain regions could help mitigate this. The heatmap shown in figure 3 gives the main affected regions of brain which incudes the hippocampus, amygdyla and parietal regions of the brain.

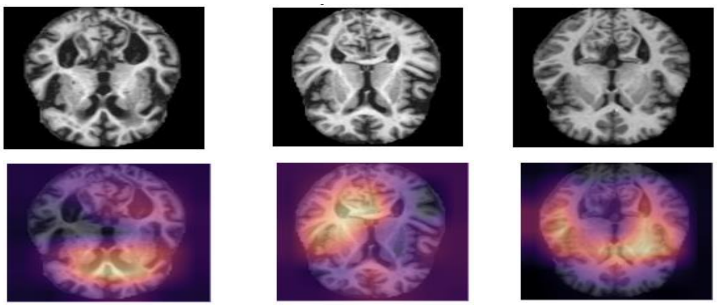

Figure 3: Heat Map of very mild, moderate and mild demented generated using gradcam.

4. Experiment and results

A total of 6400 images was used out of which 896 Mild demented, 64 Moderate demented, 3200 Non demented , 2240 very mild demented. We measured the performance of our algorithm using 1013 test images out of which 139 Mild demented, 10 Moderate demented, 530 Non demented , 334 very mild demented. We obtained an accuracy of 99% on the test data, which is remarkable achievement when compared to existing state of art. VGG16 combined with FASTAI enabled us to give such a good performance for the four way classification of alzhiemer's disease. The confusion metrics was computed as given in the figure 4 using which Precison, Recall and F1 score was computed for further analysis of the classification task a given in

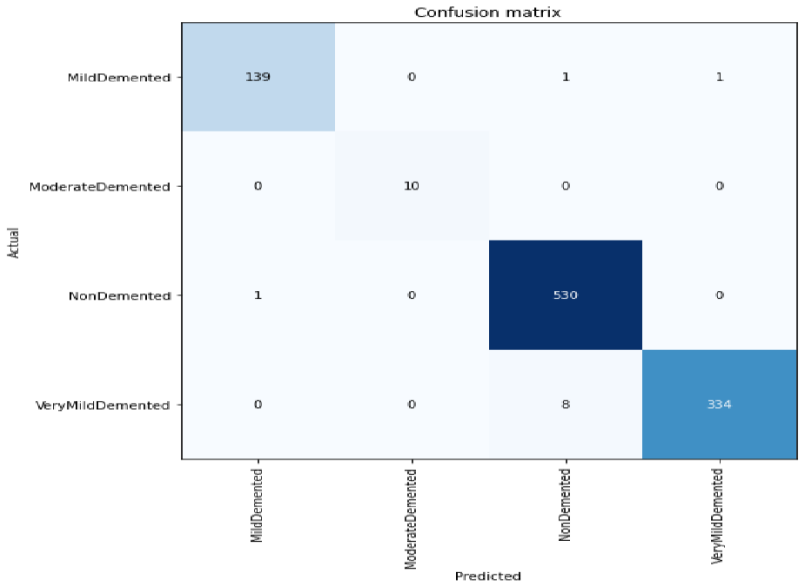

Figure 4: Confusion Matrix of 4 way classification.

Table 1: Performance measures.

	Class labels	Precison	Recall	F1Score
4 way classification	**Mild Demented**	0.992	0.985	0.98
	Moderate Demented	1	1	1
	Non Demented	0.983	0.998	0.99
	Very Mild Demented	0.997	0.976	0.98

For the training process the learning rate of 5e-4 was chosen which helped to attain smooth exponentially decreasing curve for training and validation losses and an exponentially increasing curve for training and testing accuracy as shown in Figure 5. FASTAI helped to finish the training process in very small number of epochs. Selection of 32 size batches also enabled to give good performance of the

algorithm. SGD combined with Nestrov Momentum was used as the optimizer which prevented the algorithm from falling into local minimum and converge in lesser number of iterations

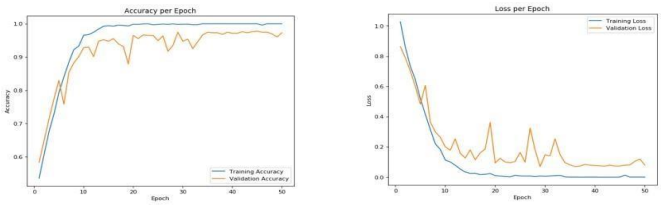

Figure 5: Graph of training and testing accuracy with epochs(loss).

5. Conclusion and Future work

In this Work, we used the basic VGG16 model with Fastai to classify Alzheimer's from MRI images . Transfer learning technique is used to avoid the expensive training from scratch and to get higher efficiency with limited number of dataset. VGG16 originally trained on Imagenet was trained with MRI images for Alzhiemer's Disease classification. The proposed work was able to give an accuracy of 99% on test data with very small misclassifications on normal and very mild demented. The heat map generated using GradCam has given a clear picture of brain affected areas for the three categories of the disease. Future work includes using datas from other modalities like PET, fMRI to improve the performance.

6. Acknowledgement

We acknowledge our gratitude to the use of Alzheimer's disease (4 class of images) and the data derived from Kaggle database. We also thank the anonymous referees for their useful suggestions. This research was supported by the electronics and communication engineering department that was provided Bannari Amman Institute of technology, Erode.

8. References

[1] A. Gupta, M. Ayhan, and A. Maida 2013 Natural image bases to represent neuroimaging data, *International Conference on Machine Learning*, vol 28, pp. 987–994.

[2] S. Sarraf, G. Tofighi, D. DeSouza and J. Anderson 2016, DeepAD:Alzheimer's Disease Classification via Deep Convolutional Neural Networks using MRI and fMRI, *bioRxiv*

[3] A. Farooq, S. Anwar, M. Awais and S. Rehman 2017 A deep CNN based multi-class classification of Alzheimer's disease using MRI, *IEEE International Conference on Imaging Systems and Techniques (IST)*, pp. 1-6,

[4] R. Jain, N. Jain, A. Aggarwal and D. Jude Hemanth 2019 Convolutional neural network based Alzheimer's disease classification from magnetic resonance brain images, *Cognitive Systems Research*, vol 57, pp.147-159

[5] T. Altaf and S. Anwar and Nadia Gul and M. Majid and Muhammad 2017 Multi-class Alzheimer Disease Classification using Hybrid Features" *Future Technologies Conference, Vancour Canada*

[6] Frisoni, G., Fox, N., Jack, C. et al. 2010 The clinical use of structural MRI in Alzheimer disease. Nat Rev Neurol **6,** pp. 67–77

[7] M. Shahbaz, S. Ali, A. Guergachi, A. Niazi and A. Umer 2019 Classification of Alzheimer's Disease using Machine Learning Techniques", *8th International Conference on Data Science, Technology and Applications*

[8] Basheera S, Sai Ram MS.2019 Convolution neural network-based Alzheimer's disease classification using hybrid enhanced independent component analysis based segmented gray matter of T2

weighted magnetic resonance imaging with clinical valuation. *Alzheimers Dement*.

[9] F. Liu and C. Shen. 2014 Learning deep convolutional features for mri based alzheimer's disease classification".*arXiv:1404.3366*

[10] Csernansky JG, Wang L, Swank J, Miller JP, Gado M, McKeel D, Miller MI, Morris JC 2005. Preclinical detection of Alzheimer's disease: hippocampal shape and volume predict dementia onset in the elderly. *Neuroimage*, pp.783-92.

[11] Rathore S, Habes M, Iftikhar MA, Shacklett A, Davatzikos C. 2107 A review on neuroimaging based classification studies and associated feature extraction methods for Alzheimer's disease and its prodromal stages. *Neuroimage*, pp. 530-548

[12] Plant C, Teipel SJ, Oswald A, Böhm C, Meindl T, Mourao-Miranda J, Bokde AW, Hampel H, and Ewers M. 2010 Automated detection of brain atrophy patterns based on MRI for the prediction of Alzheimer's disease. *Neuroimage*.

[13] R. Brookmeyer, E. Johnson, K. Ziegler-Graham, and H. M. Arrighi, 2007 Forecasting the global Burden of Alzheimer's disease, *Alzheimer's & dementia*, vol. 3, pp. 186–191

[14] S. Wang, H. Wang, Y. Shen and X. Wang, 2018 Automatic Recognition of Mild Cognitive Impairment and Alzheimer's Disease Using Ensemble based 3D Densely Connected Convolutional Networks, *17th IEEE International Conference on Machine Learning and Applications (ICMLA)*, pp. 517-523

[15] Zachary Burns, Derrick Cosmas, Bryce Smith, 2019 Early Detection of Alzheimer's Disease Through Machine Learning in MRI Scans, *University of California San Diego*,

[16] M. Hon and N. M. Khan, 2017 Towards Alzheimer's disease classification through transfer learning, *IEEE International Conference on Bioinformatics and Biomedicine (BIBM)*, pp. 1166-1169,.

[17] S. Sarraf, G.Tofighi 2016 Classification of Alzheimer's Disease Using fMRI Data and Deep Learning Convolutional Neural Networks, *arXiv:1603.08631*

[18] Xin Zhang, Liangxiu Han, Wenyong Zhu, Liang Sun, Daoqiang Zhang 2020,An Explainable 3D Residual Self-Attention Deep Neural Network FOR Joint Atrophy Localization and Alzheimer's Disease Diagnosis using Structural MRI, *arXiv:2008.04024*

[19] Visser, P., Scheltens, P., Verhey, F. *et al.* 1999 Medial temporal lobe atrophy and memory dysfunction as predictors for dementia in subjects with mild cognitive impairment. *J Neurol* 246**,** pp.477–485 .

[20] C. D. Billones, O. J. L. D. Demetria, D. E. D. Hostallero and P. C. Naval, 2016 DemNet: A Convolutional Neural Network for the detection of Alzheimer's Disease and Mild Cognitive Impairment," *IEEE Region 10 Conference (TENCON)*, pp. 3724-3727,

[21] S Kaliyugarasan, M Kocinski, A Lundervold , 2020 2D and 3D U-Nets for skull stripping in a large and heterogeneous set of head MRI using fastai," *NIK 2020 Conference*

[22] Selvaraju R, De M Cogswell A, 2016 "Grad cam visual explanations from deep networks via gradient based localization. Interna tional Journal of Computer Vision". *Springer*, pp 336–359