

SURVEY ON ALZHEIMER'S DISEASE

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ABSTRACT

Alzheimer's disease (AD) is one of the type of dementia. This is one of the harmful disease which can lead to death and yet there is no treatment. There is no current technique which is 100% accurate for the treatment of this disease. In recent years, Neuroimaging combined with machine learning techniques have been used for detection of Alzheimer's disease. Based on our survey we came across many methods like Convolution Neural Network(CNN) where in each brain area is been split into small three dimensional patches which acts as input samples for CNN. The other method used was Deep Neural Networks(DNN) where the brain MRI images are segmented to extract the brain chambers and then features are extracted from the segmented area. There are many such methods which can be used for detection of Alzheimer's Disease.

1. INTRODUCTION

Alzheimer's sickness (AD) is the most frequent shape of dementia, which is a innovative talent ailment by and large happening in the late life. Comparing with the patient's preceding functions, a decline in reminiscence and different cognitive features is referred to as a major dementia syndrome. There are three different types of AD: preclinical, Mild Cognitive Impairment and Dementia. Preclinical ability early onset of Alzheimer's and so occurs to these youthful and under sixty five years. It's a uncommon case in scientific records with 5% of human beings catching these early onsets of Alzheimer's. Mild Cognitive Impairment (MCI) is a transitional stage[1]. This is related with language, thinking, reminiscence adjustments and judgment higher than the everyday condition. Finally, dementia is major category of brain diseases. The early stage of dementia will have some frequent symptoms. It has lengthy time period impact on linguistic capacity and it will undergo upon every day functioning in a person's lifetime. Dementia will reason one-of-a-kind conditions, which consist of Huntington's disease, Creutzfeldt-Jakob sickness (CJD), Lewy body disease and vascular dementia, Parkinson's disease, and Wernicke-Korsakoff syndrome[2]. Medical imaging performs a imperative function in dementia. Imaging biomarkers are a set of indications computed from photograph modalities and can be used for the early detection of AD diseases. Some usually used scientific pictures to analysis dementia at an early stage consist of magnetic resonance imaging (MRI), positron emission tomography (PET)[3], Cerebro-spinal Fluid (CSF), single-photon emission computed tomography (SPECT), Computerized Tomography (CTscans), electroencephalogram(EEG)signal[4][5]. It assesses the total brain signals. Structural MRI makes use of radio waves and a magnetic area to picture tissues and organs in the human body. This approach offers many advantages, which include higher smooth tissue contrast, decrease cost, higher accessibility and regional atrophy. Structural MRI picture are obtained from Alzheimer's sickness Neuroimaging Initiative (ADNI) for figuring out AD progression. Functional PET having some a variety of radioactive tracers, for example, 18C- Pittsburgh Compound (11C-PiB), and 2-[18F] Fluoro-2-deoxy-D-glucose (FDG) can become aware of the moderate adjustments in amyloid deposition or cerebral metabolism prior to anatomical modifications is a

symptomatological diagnosis of dementia. Functional SPECT is analogous to PET pics via the usage of a radioactive isotope and imaging gamma rays from it[6]. SPECT scan is much less highly-priced than PET scans however has decrease spatial decision compared to PET scans. In clinical research, obtaining the data sets is very difficult, that too acquiring 3-d dataset photographs is ordinarily unexplored. Comparatively low extent of work is absolutely based on visible evaluation of slice by slice search of 3-d datasets for affected illnesses patterns. This will require sizeable knowledge, effort, fee and time. Inasmuch as the doctor's opinion, computer aided classification and identification of dementia is nonetheless the most promising device at an early stage. Those processes are categorized into three categories: differentiating AD from NC figuring out the exclusive levels of AD: MCI from AD and AD from FTD. There are many databases reachable for diagnosis of AD, together with the Alzheimer's Disease Neuroimaging Initiative (ADNI)[7] and Open Access Series of Imaging Studies (OASIS)[8]. These databases are broadly used for identification and classification of dementia an early stage in the research. The next section will explain about the related work on Alzheimer's disease, conclusion and references.

2. RELATED WORK

Developing an Alzheimer's Disease detection and classification model is a pretty challenging task. But there are some remarkable research work in this area.

2.1 Convolution Neural Network

In Yanqing Zhang, et. al [26]; Alzheimer's disease detection and classification is done when the input (T1-weighted MRI scans from OASIS dataset) is passed through a stem layer. This stem layer includes several 3*3 convolution layers, 1*1 convolution layer, and max pooling layer. In the convolution layer, there are two types of modules: Inception and Reduction, Inception has three modules and Reduction has two modules. The input and output of all these modules pass through various filter concatenation process. They have redesigned the final softmax layer for Alzheimer's disease detection and classification. Nondemented, very mild, mild, and moderate AD are the four different output classes of the softmax layer. MRI image is taken as input by the network and it extracts layer- wise feature representation from the first stem layer to the last drop-out layer. Based on this mentioned feature representation, the input MRI image is classified to any of the four output classes. They have also applied data augmentation techniques such as reflection and scaling. This Silvia Basaia et.al [15] utilize single MRI and deep neural networks. An independent dataset of 3D T1-weighted images was obtained from ADNI and Milan. 3D T1- weighted images from both datasets were normalized to the MNI space using Statistical Parametric Mapping and the Diffeomorphic Anatomical Registration Exponentiated Lie Algebra (DARTEL) registration method. Given the volumetric nature of MR images, a network architecture that uses 3D convolutions was developed first. Then inputs were normalized 3D T1-weighted images and the outputs to be predicted were subject groups. The network used in their study differs from the standard CNNs as max-pooling layers were replaced by standard convolutional layers with a stride of 2. To improve the performance of the classifier, a transfer learning was applied, i.e., weights of the CNN used to classify ADNI AD vs HC(healthy controls) were transferred to the other CNNs and used as (pre-trained) initial weights. CNN was finally used to classify raw images of the testing set available. CNN's performance was evaluated by several performance measures such as sensitivity, specificity, and accuracy. David A. Wolk et. al [25] included data from the ADNI (<http://adni.loni.usc.edu>) and AIBL (www.aibl.csiro.au) cohorts, consisting of baseline MRI scans and Hippocampus extraction was done to this dataset. These hippocampal data were used to extract features and build the prognostic model A deep learning model of convolutional neural networks was used for informative feature extraction. A time-to-event prognostic model based on deep imaging features estimates overall risk scores to progress to AD dementia for individuals. In Dan Pan et. al[21] Here, they developed a three-axis multi-slice (i.e. sagittal, coronal, and transversal slices) MRI classifier using CNN and ensemble learning. In the standard MNI space, the intersection points were determined by the most discriminable three-axis slices that were located in some identified brain regions with the help of Brainnetome Atlas. This Jun Chen et. al [9] used five components for Detection of Alzheimer's Disease from Narrative Speech. Firstly, Embedding layer will map each word from the

input transcript into a continuous vector. Secondly, GRU layer applies bidirectional GRU on the top of the word embedding layer to get contextual word representations. Thirdly, CNN layer which performs one-dimensional convolution on embedded word sequence to extract local n-gram patterns from transcript. Fourth, Attention layer takes the input of the output of the previous layer (feature map from CNN or contextual word representations from biGRU) and calculates a weight vector that measures the importance of each feature and computes the transcript-level vector as a weighted sum of features. Last is the Output layer which concatenates transcript-level vectors from CNN and GRU branches, and feed the resulting vector to a fully-connected layer for softmax classification.

2.2 Deep Neural Network

In Kajal Kiran Gulhare, et.al[12] DNN classification is considered to be a tool for Alzheimer disease detection. Minimum error rate is obtained from DNN with three hidden layers and softmax layer as an output layer which is superior to that obtained from the SVM and backpropagation classifier. The MRI data was accessed and stored in the database and data pre-processing technique was used for removing non-relevant information and for better interpretation. The image segmentation methods were applied on the image data to extract different features of the data. The attributes were extracted from the data and artificial neural network based classification method was applied on extracted data to verify feasibility of the classifier. The niblack-thresholding segmentation algorithm was used for the segmentation process. This Kim- Han Thung, et.al[18] used multi-task deep learning of incomplete data, where prediction tasks that are associated with different modality combinations are used to improve the performance of each task. They combined a multi-input multi-output deep learning framework and trained a network by updating its weights based on the availability of modality data. ADNI dataset was used and Multi-Task Deep Learning (MTDL) framework contains two types of input (one for each modality) and three types of output (one for each classification task). The architecture consists of three layers, i.e., input layer, hidden layers, and output layers. Figure 1 shows an overview of MTDL framework for two incomplete modalities.

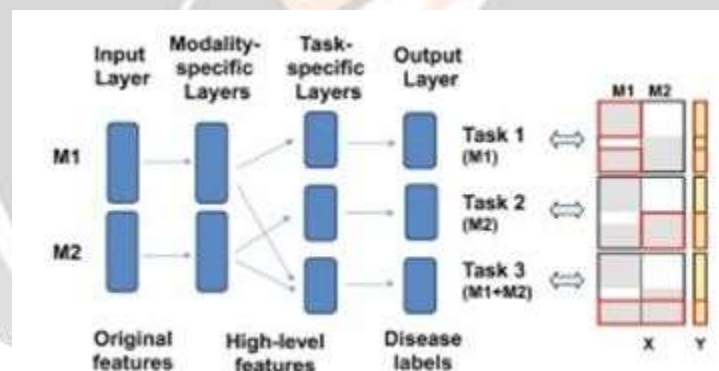


Fig-1: Multi task deep learning(MTDL) via multi-input multi-output neural network

Nicola Amoroso, et.al[19] Here they used classification strategy based on Random Forest feature selection and Deep Neural Network. Random Forest classifier evaluates the feature importance in terms of mean decrease of accuracy and they are the ensembles of tree classifiers which provides a direct multi-class model. A standard configuration was adopted with 500 trees and 20 features which was randomly selected. Hippocampal volumes was found to be the best performing features and the selected features from that was used to train a Deep Neural Network. Feedforward DNN was used, which learned to map the feature representation of each patient in the four aforementioned classes. In fact, the classification results obtained by DNN allowed the Bari Medical Physics Group(BMPG) to obtain one of the most accurate prediction in the participants roster.

2.3 Deep Convolutional Neural Network(DCNN)

Joythi Islam,et.al[9] have proposed a method which performs four basic operations- convolution, batch normalization, verified linear unit and pooling. They follow a particular connectivity known as dense connectivity, where each layer is connected to other layer. Softmax layer is used for classification which has four different output classes: non- demented, very mild, mild and moderate AD. From the obtained MRI data patches

were created and these patches were given as input to the proposed network. The size of each patch which used was of the size 112*112 and to handle the imbalance in the data set cost sensitive training was used. A cost matrix ξ was used to modify the output of the last layer of the network. If o denotes output of the individual model, p denotes the desired class and L denotes the loss function, then y denotes the modified output:

$$y_i = L(\xi p, o_i), : y_{ij} \geq y_{ij} \forall j \neq p \quad (1)$$

C.H.Suh, et.al [6] they have used deep learning

based automatic brain segmentation and classification algorithm for accurate diagnosis of AD. TI-weighted brain MRI images have been used here. A two-step based DCNN was used to perform brain parcellation followed by 3 classifier techniques including XG-Boost for disease prediction. All these classification techniques were performed using 5-fold cross-validation. XG-Boost method was compared with logistic regression and Support Vector Machine by calculating the areas under the curve for differentiating AD from MCI and MCI from healthy brain. The conclusion says that TI-weighted brain images are widely available and best for prediction of Alzheimer's Disease.

2.4 Deep Learning with Modified k-sparse auto-encoder(KSA)

In Pushkar Bhatkoti, et.al [11] Multiclass Deep Learning Framework with Modified k-sparse Autoencoder Classification is proposed which was used to detect Alzheimer disease at early stages. It compares the modified approach to non-modified k-sparse approach. The KSA algorithm is based on the learning of representations and performance is attained on categorization tasks. Autoencoders are feature extraction algorithms. An autoencoder uses an activation function $y = f(Px + b)$ [11]. They used three different inputs (MRI, CSF and PET) and processed them to get the desired results. A practical approach with actual MRI images from patient screening was used in the research and compared with data from ADNI. The MRI scans were reprocessed by correcting errors and by skull strip to obtain the underlying tissues. The images were normalized and smoothed and region of interest were obtained and it was used to prepare datasets. Binary classification results in Figure 2 shows that KSA performed better than the two other previous approaches. The percentage was based on mean and standard deviation values obtained.

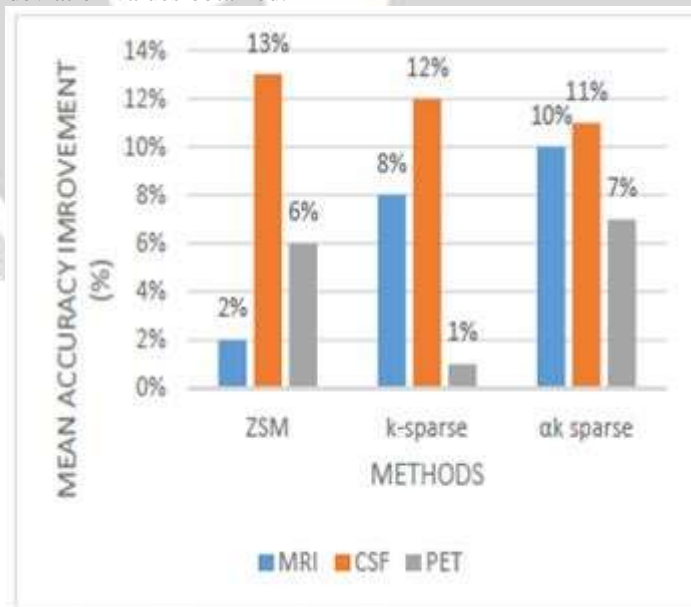


Fig-2: Comparative Accuracy Improvement

2.5 3D Convolutional Neural Network

In Simeon Spasov et.al[13] Novel deep learning architecture is presented based on dual learning and an ad hoc layer for 3D separable convolutions, which aims at identifying those people with MCI who have a high risk of developing Alzheimer disease. They combined magnetic resonance imaging (MRI), demographic, neuropsychological, and APOe4 genotyping data as input measures where the same network layers are used to extract representations from the input biomarkers for both the MCI-to-AD conversion task and the AD/HC classification problem. All the analyses were performed on the Alzheimer's Disease Neuroimaging Initiative (ADNI) database and they also combined Tensorflow and Keras libraries with their own 3D implementation of 3D separable convolutions.

3. CONCLUSIONS

A complete study was done in different categories on detection of Alzheimer's disease which explained about the methods used, datasets acquired and many more. There were few drawbacks from some of the papers like overfitting many parameters where small sets of data had to be used, diagnosis is not done at early stage which might lead to risk of the patients life and many more. Currently none of the existing methods provide 100% accuracy. In fact new technologies can be used for diagnosis of Alzheimer's disease at early stage which is one of the major existing problem in medical area.

4. REFERENCES

- [1]. Alzheimer's Association. "2014 Alzheimer's disease facts and figures." *Alzheimer's & Dementia* 10, no. 2 (2014): e47-e92
- [2]. Seixas, Flávio Luiz, Bianca Zadrozny, Jerson Laks, Aura Conci, and Débora Christina Muchaluat Saade. "A Bayesian network decision model for supporting the diagnosis of dementia, Alzheimer's disease and mild cognitive impairment." *Computers in biology and medicine* 51 (2014): 140-158.
- [3]. Cai, Weidong, Dagan Feng, and Roger Fulton. "Content-based retrieval of dynamic PET functional images." *IEEE Transactions on Information Technology in Biomedicine* 4, no. 2 (2000): 152-158.
- [4]. Silverman, Daniel HS. "Brain 18F-FDG PET in the diagnosis of neurodegenerative dementias: comparison with perfusion SPECT and with clinical evaluations lacking nuclear imaging." *Journal of Nuclear Medicine* 45, no. 4 (2004): 594- 607.
- [5]. Aël Chetelat, G., and Jean-Claude Baron. "Early diagnosis of Alzheimer's disease: contribution of structural neuroimaging." *Neuroimage* 18, no. 2 (2003): 525-541.
- [6]. Ramírez, Javier, J. M. Górriz, Diego Salas- Gonzalez, A. Romero, Míriam López, Ignacio Álvarez, and Manuel Gómez-Río. "Computer-aided diagnosis of Alzheimer's type dementia combining support vector machines and discriminant set of features." *Information Sciences* 237 (2013): 59-72.
- [7]. Hua, Xue, Alex D. Leow, Neelroop Parikhshak, Suh Lee, Ming-Chang Chiang, Arthur W. Toga, Clifford R. Jack Jr, Michael W. Weiner, Paul M. Thompson, and Alzheimer's Disease Neuroimaging Initiative. "Tensor-based morphometry as a neuroimaging biomarker for Alzheimer's disease: an MRI study of 676 AD, MCI, and normal subjects." *Neuroimage* 43, no. 3 (2008): 458-469.
- [8]. Marcus, Daniel S., Tracy H. Wang, Jamie Parker, John G. Csernansky, John C. Morris, and Randy L. Buckner. "Open Access Series of Imaging Studies (OASIS): cross-sectional MRI data in young, middle aged, nondemented, and demented older adults." *Journal of cognitive neuroscience* 19, no. 9 (2007): 1498-1507.
- [9]. Chen, Jun, Ji Zhu, and Jieping Ye. "An Attention-Based Hybrid Network for Automatic Detection of Alzheimer's Disease from Narrative Speech." In *INTERSPEECH*, pp. 4085-4089. 2019.
- [10]. Ortiz, Andres, Jorge Munilla, Juan M. Gorriz, and Javier Ramirez. "Ensembles of deep learning architectures for the early diagnosis of the Alzheimer's disease." *International journal of neural systems* 26, no. 07 (2016): 1650025.
- [11]. Bhatkoti, Pushkar, and Manoranjan Paul. "Early diagnosis of Alzheimer's disease: A multi-class deep learning framework with modified k-sparse autoencoder classification." In *2016 International Conference on Image and Vision Computing New Zealand (IVCNZ)*, pp. 1- 5. IEEE, 2016.
- [12]. Gulhare, Kajal Kiran, S. P. Shukla, and L.K. Sharma. "Deep Neural Network Classification method to

- Alzheimer's Disease Detection." *International Journals of Advanced Research in Computer Science and Software Engineering* 7, no. 6 (2017): 1-4.
- [13]. Spasov, Simeon, Luca Passamonti, Andrea Duggento, Pietro Liò, Nicola Toschi, and Alzheimer's Disease Neuroimaging Initiative. "A parameter-efficient deep learning approach to predict conversion from mild cognitive impairment to Alzheimer's disease." *Neuroimage* 189 (2019): 276-287.
- [14]. Suh, C. H., W. H. Shim, S. J. Kim, J. H. Roh, J-H. Lee, M-J. Kim, S. Park et al. "Development and Validation of a Deep Learning-Based Automatic Brain Segmentation and Classification Algorithm for Alzheimer Disease Using 3D T1- Weighted Volumetric Images." *American Journal of Neuroradiology* 41, no. 12 (2020): 2227-2234.
- [15]. Basaia, Silvia, Federica Agosta, Luca Wagner, Elisa Canu, Giuseppe Magnani, Roberto Santangelo, Massimo Filippi, and Alzheimer's Disease Neuroimaging Initiative. "Automated classification of Alzheimer's disease and mild cognitive impairment using a single MRI and deep neural networks." *NeuroImage: Clinical* 21 (2019): 101645.
- [16]. Yamanakkanavar, Nagaraj, Jae Young Choi, and Bumshik Lee. "MRI Segmentation and Classification of Human Brain Using Deep Learning for Diagnosis of Alzheimer's Disease: A Survey." *Sensors* 20, no. 11 (2020): 3243
- [17]. Islam, Jyoti, and Yanqing Zhang. "Early Diagnosis of Alzheimer's Disease: A Neuroimaging Study with Deep Learning Architectures." In *Proceedings of the IEEE conference on computer vision and pattern recognition workshops*, pp. 1881-1883. 2018.
- [18]. Thung, Kim-Han, Pew-Thian Yap, and Dinggang Shen. "Multi-stage diagnosis of Alzheimer's disease with incomplete multimodal data via multi-task deep learning." In *Deep learning in medical image analysis and multimodal learning for clinical decision support*, pp. 160-168. Springer, Cham, 2017.
- [19]. Amoroso, Nicola, Domenico Diacono, Annarita Fanizzi, Marianna La Rocca, Alfonso Monaco, Angela Lombardi, Cataldo Guaragnella, Roberto Bellotti, Sabina Tangaro, and Alzheimer's Disease Neuroimaging Initiative. "Deep learning reveals Alzheimer's disease onset in MCI subjects: results from an international challenge." *Journal of neuroscience methods* 302 (2018): 3-9.
- [20]. Islam, Jyoti, and Yanqing Zhang. "Brain MRI analysis for Alzheimer's disease diagnosis using an ensemble system of deep convolutional neural networks." *Brain informatics* 5, no. 2 (2018): 2.
- [21]. Pan, Dan, Yin Huang, An Zeng, Longfei Jia, Xiaowei Song, and Alzheimer's Disease Neuroimaging Initiative (ADNI). "Early Diagnosis of Alzheimer's Disease Based on Deep Learning and GWAS." In *International Workshop on Human Brain and Artificial Intelligence*, pp. 52-68. Springer, Singapore, 2019.
- [22]. Feng, Wei, Nicholas Van Halm-Lutterodt, Hao Tang, Andrew Mecum, Mohamed Kamal Mesregah, Yuan Ma, Haibin Li et al. "Automated MRI-Based Deep Learning Model for Detection of Alzheimer's Disease Process." *International Journal of Neural Systems* 30, no. 06 (2020): 2050032.
- [23]. Ding, Yiming, Jae Ho Sohn, Michael G. Kawczynski, Hari Trivedi, Roy Harnish, Nathaniel W. Jenkins, Dmytro Lituiev et al. "A deep learning model to predict a diagnosis of Alzheimer disease by using 18F-FDG PET of the brain." *Radiology* 290, no. 2 (2019): 456- 464.
- [24]. Liu, Siqi, Sidong Liu, Weidong Cai, Sonia Pujol, Ron Kikinis, and Dagan Feng. "Early diagnosis of Alzheimer's disease with deep learning." In *2014 IEEE 11th international symposium on biomedical imaging (ISBI)*, pp. 1015-1018. IEEE, 2014.
- [25]. Li, Hongming, and Yong Fan. "Early prediction of Alzheimer's disease dementia based on baseline hippocampal MRI and 1- year follow-up cognitive measures using deep recurrent neural networks." In *2019 IEEE 16th International Symposium on Biomedical Imaging (ISBI 2019)*, pp. 368-371. IEEE, 2019.
- [26]. Islam, Jyoti, and Yanqing Zhang. "A novel deep learning based multi-class classification method for Alzheimer's disease detection using brain MRI data." In *International Conference on Brain Informatics*, pp. 213-222. Springer, Cham, 2017.