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Prediction of Alzheimer's Disease with Deep Learning

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Abstract - *Despite decades of research, there is still no definitive test to diagnose Alzheimer's disease , so a careful medical evaluation is needed to help lead to a diagnosis. Imaging plays an important role for the early diagnosis of AD. Alzheimer's Disease (AD) diagnosis can be carried out by analyzing functional or structural changes in the brain. Functional changes associated to neurological disorders can be figured out by positron emission tomography (PET) as it allows to study the activation of certain areas of the brain during specific task development. On the other hand, neurological disorders can also be discovered by analyzing structural changes in the brain which are usually assessed by Magnetic Resonance Imaging (MRI). However, functional and structural data can be fused out in order to improve the accuracy and to diminish the false positive rate. In this paper we present a method for the diagnosis of AD which fuses multi-modal image (PET and MRI) with the help of naive bayes classifier.*

Key Words: Alzheimer's disease, neurological disorders, positron emission tomography, Magnetic Resonance Imaging, multi-modal image.

1. INTRODUCTION

Alarmingly increasing prevalence of Alzheimer's disease (AD) due to the aging population in developing countries, combined with lack of standardized and conclusive diagnostic procedures, make early diagnosis of Alzheimer's disease a major public health concern.

Alzheimer's disease is a progressive disease that destroys memory and other important mental functions. At first, some- one with Alzheimer's disease may notice mild confusion and difficulty remembering. Eventually, people with the disease may even forget important people in their lives and undergo dramatic personality changes. Alzheimer's disease is the most common cause of dementia a group of brain disorders that cause the loss of intellectual and social skills. In Alzheimer's disease, the brain cells degenerate and die, causing a steady decline in memory and mental function.. Alzheimer's disease is caused by a combination of genetic, lifestyle and environmental factors that affect the brain over time.

Less than 5 % of the time, Alzheimer's is caused by specific genetic changes that virtually guarantee a person will develop the disease. A brain affected by Alzheimer's disease has many fewer cells and many fewer connections among surviving cells than does a healthy brain. As more and more brain cells die, Alzheimer's leads to significant brain shrinkage. When doctors examine Alzheimer's brain tissue under the microscope, they see two types of abnormalities that are considered hallmarks of the disease:

1.1 Plaques:

These clumps of a protein called beta-amyloid may damage and destroy brain cells in several ways, including interfering with cell-to-cell communication. Although the ultimate cause of brain-cell death in Alzheimer's isn't known, the collection of beta-amyloid on the outside of brain cells is a prime suspect.

1.2 Tangles:

Brain cells depend on an internal support and transport system to carry nutrients and other essential materials throughout their long extensions. This system requires the normal structure and functioning of a protein called tau. In Alzheimer's, threads of tau protein twist into abnormal tangles inside brain cells, leading to failure of the transport system. This failure is also strongly implicated in the decline and death of brain cells.

Importantly, imaging has a major role to play in improving our understanding of the disease. Together with this topo- graphical information imaging can quantify multiple different aspects of AD pathology and assess how they relate to each other and how they change over time. A variety of imaging modalities, including structural and functional magnetic resonance imaging (MRI) and positron emission tomography (PET) studies of cerebral metabolism, have shown character- changes in the brains of patients with Alzheimer disease in prodromal and even presymptomatic states. Default mode network (DMN) imaging appears to distinguish AD, MCI, and controls well, and it may complement positron emission tomography (PET) scanning or prove to be more sensitive.

2. DETAILS EXPEIMENTAL

2.1 Materials

In this work, we used the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset for performance evaluation. The ADNI was launched in 2003 by the National Institute on Aging (NIA), the National Institute of Biomedical Imaging and Bioengineering (NIBIB), the Food and Drug Adminis- tration (FDA), private pharmaceutical companies and non- profit organizations, with a $60 million 5-year public private partnership. The primary goal of ADNI was to demonstrate whether MRI, PET, other biological-markers, and clinical & neuropsychological assessment could be combined to measure the progression of MCI and early AD. The pipeline of the proposed framework is illustrated in Figure. In this study, MR and PET data are used as two input neuroimaging modalities .The dataset is divided into a training set and atesting set. The PET images were aligned to the corresponding MR image. The proposed AD recognition system can be completed in two processes including system training and practical testing. The training mainly builds the system based on designing and training data. The test will give recognition result based on current input data. In particular, the recognition algorithm starts from MRI data as input, pre-processes the data to increase recognition accuracy, then completes the recognition using convolutions neural networks. The following sections describe these steps.

2.2 Data Collection & Pre-Processing

The proposed system is built and tested with the MRI data acquired from Alzheimer's Disease Neuroimaging Initiative (ADNI) database. The primary goal of ADNI has been to test whether serial MRI, PET, other biological markers, and clinical and neuropsychological assessment can be combined to measure the progression of mild cognitive impairment and early AD. AXIAL T2 FLAIR MR images are selected. MRI images brain in axial, coronal and sagittal planes. MRI scans can produce detailed pictures of organs, soft tissues, bone and other internal body structure.

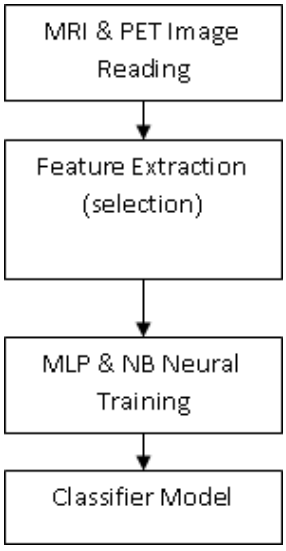

Fig 1: Training Part

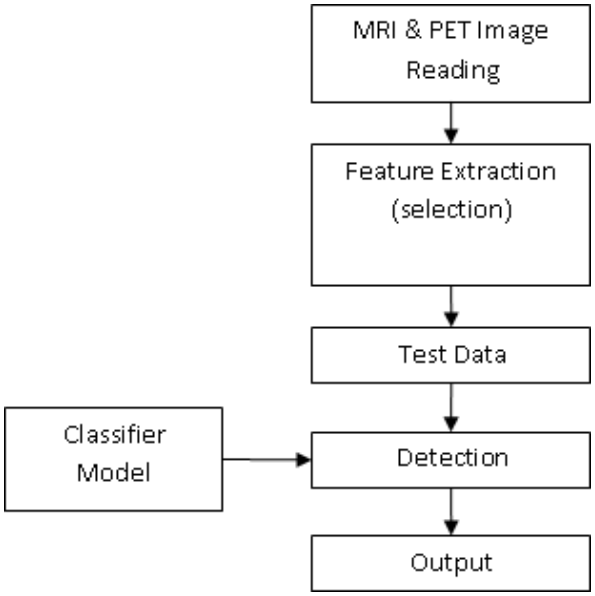

Fig-2: Testing Part

2.2.1 Morphological Operations

Artifacts introduced during acquisition and undesired tissues affect the processing quality and lead to inaccurate diagnosis. Thus, an important preprocessing step is skull stripping where the brain tissue is segmented from the skull. Since the manual segmentation is very time consuming and prone to errors, various methods have been developed to automatically remove extra-cerebral tissues without human intervention. Morphometric studies require a preprocessing procedure to isolate the brain from extra-cranial. To analyze geometrical structures such as size, shape, connectivity, mathematical morphology is a tool used which is based on set theory. It was developed originally for binary images but can be used for grayscale and color images. There are four basic operations of mathematical morphology: dilation, erosion, opening and closing. Dilation is defined as the maximum value in the window. Hence the image after dilation will be brighter or increased in intensity. It also expands the image and mainly used to fill the spaces. Erosion is just opposite to dilation. It is defined as the minimum value in the window .The image after dilation will be darker than the original image. It shrinks or thins the image. Opening and closing both parameters are formed by using dilation and erosion. In opening, firstly image will be eroded and then it will be followed by dilation. In closing, the first step will be dilated and then result of this is followed by erosion.

Conversion to binary image:

The input image is converted to binary image. Method automatically performs reduction of a gray level image to

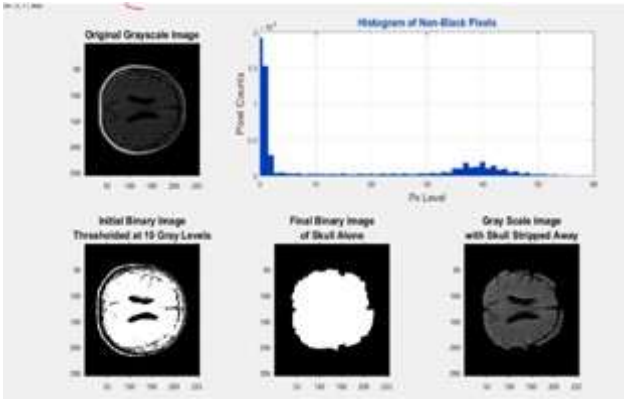

Fig-3: Morphological Operations

a binary image. The algorithm considers the image as two classes of pixels, foreground pixels and background pixels. Optimum threshold is obtained which separates the two classes so that their intra-class variance is minimal and theirinter-class variance is maximal.

Creation of mask:

Brain is the largest connected component. This component is extracted from the binary image. Dilation and erosion operations are performed to preserve the minute features of the brain in the resultant image. By filling the holes, the brain becomes a complete connected component. Superimposition: The final skull stripped image is obtained by superimposing the mask on the input image.

2.2.2Multimodal Data Fusion:

MRI Images

The 2 MR image of same person compared for getting output. This output is applied to classifier. MLP classifier used for getting better result. The MLP is divided into three layers: the input layer, the hidden layer and the output layer, where each layer in this order gives the input to the next. The extra layers gives the structure needed to recognise non- linearly separable classes. Algorithm The threshold function of the units is modified to be a function that is continuous derivative, the Sigmoid function

$$f_{net} = 1/(1xe^{k}net) \ldots\ldots(1)$$

The use of the Sigmoid function gives the extra information necessary for the network to implement the back-propagation training algorithm. Back-propagation works by finding the squared error (the Error function) of the entire network, and then calculating the error term for each of the output and hidden units by using the output from the previous neuron layer. The weights of the entire network are then adjusted with dependence on the error term and the given learning rate.

$$w_{ij}(t^1) = w_{ij}(t)^{n}\delta_{pj}o_{pj} \ldots\ldots\ldots\ldots(2)$$

PET Images

The mean intensity in the brainstem region of the FDG-PET image was the chosen reference to normalize the voxel intensities in the individual brain metabolism image because brainstem region was most unlikely to be affected by AD. The mean intensity of each patch was used as an element to form the feature vector to represent the metabolism activity, and the volume of each patch was used to represent the brain atrophy. Then output given to naive bayes classifier.

Naive Bayes Classifier is the simple Statistical Bayesian Classifier. It is called Naive as it assumes that all variables contribute towards classification and are mutually correlated. This assumption is called class conditional independence. It is also called Idiots Bayes, Simple Bayes, and Independence Bayes. They can predict class membership probabilities, such as the probability that a given data item belongs to a particular class label. A Naive Bayes classifier considers that the presence (or absence) of a particular feature (attribute) of a class is unrelated to the presence (or absence) of any other feature when the class variable is given.

The Naive Bayes Classifier technique is based on Bayesian Theorem and it is used when the dimensionality of the inputs is high. Bayesian classification is based on Bayes Theorem and Bayes Theorem is stated as below: Let X is a data sample whose class label is not known and let H be some hypothesis, such that the data sample X may belong to a specified class C. Bayes theorem is used for calculating the posterior probability P(C—X), from P(C), P(X), and P(X—C). Where P(C—X) is the posterior probability of target class. P(C) is called the prior probability of class. P(X—C) is the likelihood which is the probability of predictor of given class. P(X) is the prior probability of predictor of class.

$$P(C/X) = P(X/C).P(C)P(X) \ldots\ldots(3)$$

The Naive Bayes classifier [2] works as follows: 1. Let D be the training dataset associated with class labels. Each tuple is represented by n-dimensional element vector, X=(x1, x2, x3,....., xn). Consider that there are m classes C1, C2, C3. ,Cm. Suppose that we want to classify an unknown tuple X, then the classifier will predict that X belongs to the class with higher posterior probability, conditioned on X. i.e., the Naive Bayesian classifier assigns an unknown tuple X to the class C_i if and only if $P(Ci\,X) > P(Cj\;X)$ For $1jm$, and

ij, above posterior probabilities are computed using Bayes Theorem.

3. PERFORMANCE EVAUATION

The proposed framework was implemented on MATLAB 2016a. In experiments including multiple modalities, we com- pared the performance with only single-modal data, MR or PET, and the data fusion methods with both modalities. To avoid the lucky trials, we randomly sampled the training and testing instances from each class to ensure they have similar distributions as the original dataset. The entire network was trained and fine-tuned with the 90% of data and then tested with the rest of samples in each validation trial. The hyper- parameters of all compared methods were chosen in each validation trial using the approximate search in log-domain to obtain the best performed model. Two hidden layers were used in all neural-network based experiments because adding additional hidden layers did not show further improvements on AD classification. It is reasonable to assume that two nonlinear transformations could be ideal to represent the neuroimaging features for AD classification. The user friendly view as:

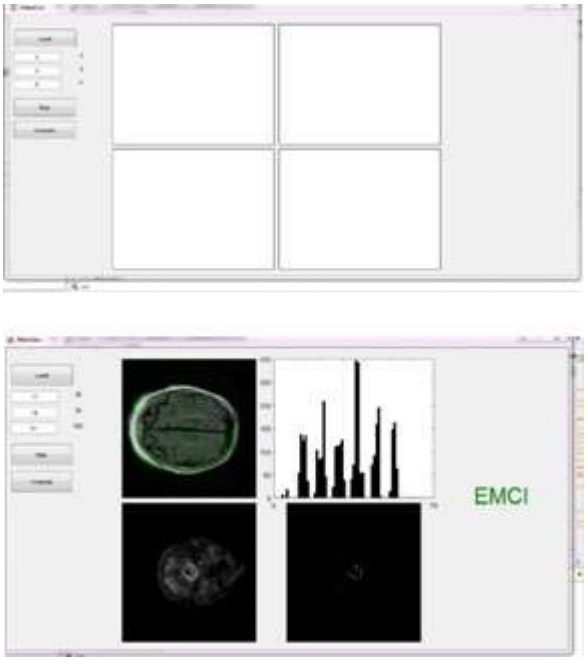

Fig-4: Input & Output

4. RESULTS & DISCUSSION

In order to measure the performance of our model in the best scientific way, sensitivity and specificity classification rule is used in our experiment. In a binary classification test, sensitivity is the ratio of predicted positive data over total true positive data, while specificity is the proportion of predicted negative data on total real negative data. In this experiment, sensitivity is the predicted high-labeled examples over all the high-labeled data in test example. And specificity is the predicted low-grade examples over all low labeled testing data .The table and graph shows each details of each parameter.

		TP	TN	FP	FN	SPE	SEN	ACC
1	NC	60	25	5	10	85.7	83.3	84.5
2	EMCI	63	26	4	7	90	86.7	88.3
3	LMCI	59	26	4	11	84.3	86.7	85.5
4	AD	59.1	25	5	11	84.4	83.3	83.9
5	LMCI	63	26	4	7	90	86.7	88.3
6	AD	62	21	9	8	88.6	70	79.3
						87.2	82.8	85

Table-1: Performance (%) of multi-class and classification

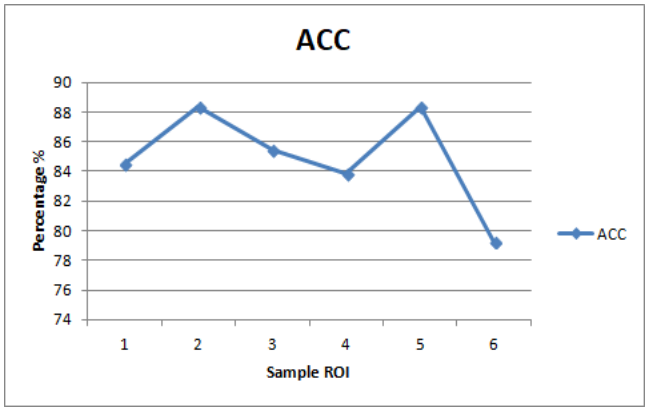

Chart-1: Accuracy

Sensitivity =TP/ (TP+FN)

=Number of Predicted High Graded Data/ Number of High Graded Data

Specificity=TN / (TN+FP)

= Number of Predicted Low Graded Data/Number of Low Gated Data

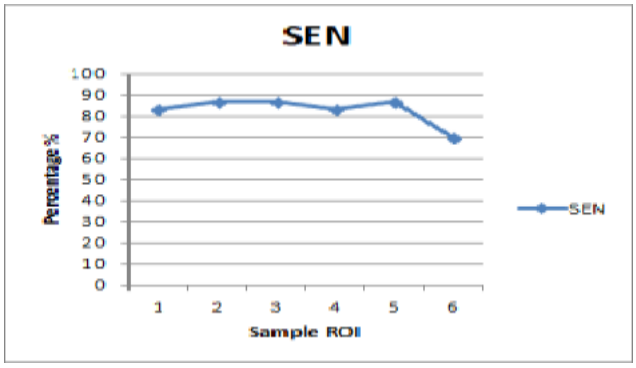

Chart-2:Sensitivity

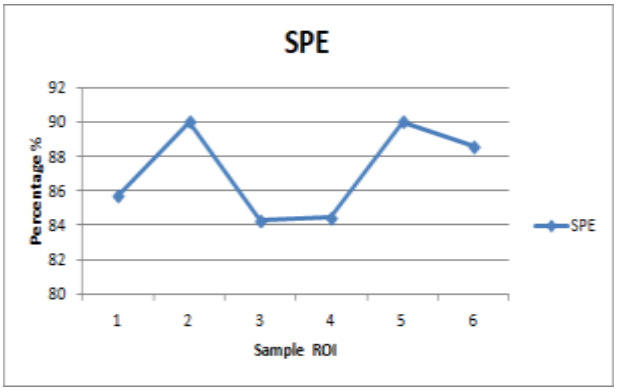

Chart-3: Specificity

In the above equation, true positives are the high-labeled data that are correctly graded and true negatives are the correctly predicted low-grade tumor slices. Whereas, false positives are the low-graded images that are classified wrongly while false negatives are the high-labeled data that are classified wrongly.

According to the definition, the sensitivity reflects how many AD cases were detected accurately. Higher the sensitivity, less AD cases were missing. The specificity reflects how many NC cases were detected accurately. Higher the specificity, less normal cases were misrecognized as AD. Using these two metrics together, the performance of the proposed method can be evaluated comprehensively

5. CONCLUSIONS

Neuroimaging methods are capable of detecting substantial brain changes, not only in subjects with AD dementia, but also in subjects in the mildly symptomatic MCI due to AD stage and even in cognitively normal subjects who might be in the preclinical stage of AD. There are imaging modality- specific changes within these clinical/preclinical stages. In the preclinical stage, Ab deposits e are already present in a substantial number of subjects.

Such changes are associated with increased grey matter AD- typical structural and functional changes at the MCI stage are reflected by changes in a variety of measures. Such measures include significant levels of amyloid PET binding in the brain, fMRI-assessed task-related medial temporal lobe hyper activation and default network dysfunction, FDG-PET- assessed temporoparietal hypometabolism, MRI-assessed medial temporal lobe atrophy and diffusion changes.

The mathematical morphological operations are applied to enhance the image contrast. It will show the clear spots of analysis to improve the image. The Applications of mathematical morphology give up a high value image and it expose most of the unidentified locations clearly.

Experimental results on the ADNI database demonstrated that method achieved significant performance improvement in AD classification compared with several state of the art methods.

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