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High Precision Diagnosis and Early Detection of Alzheimer's disease Using Functional Magnetic Resonance Imaging

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Abstract: This paper describes the high precision early diagnosis and classification of Alzheimer's disease using Functional Magnetic Resonance Imaging (fMRI). Since fMRIs records metabolic activity of brain over the time, it has excellent spatial and good temporal resolution then MRI imaging technique. To perform an early diagnosis of brain disorders such as Alzheimer's disease (AD) and Parkinson's disease (PD). To apply deep learning (DL) classification algorithms for the accurate detection of severity levels in order to begin the healing process. To improve the performance metrics of the proposed classification model in terms of Sensitivity, Specificity and accuracy. The proposed methodology is going to deal with fMRI image sets using 3D – Convolutional Neural Network (3D – CNN) is preferred to produce high accuracy. The 3D - CNN based brain disorder classification is divided into two phases such as training and testing phases. The number of images is divided into different category by using labels name such as AD, and normal brain image (NBI). In the training phase, preprocessing, feature exaction and classification with Loss function is performed to make a prediction model. Initially, label the training image set. Finally, the convolution neural network is used for automatic brain disorder classification.

Index Terms— Functional Magnetic Resonance Imaging (fMRI), Normal Brain Image (NBI), Alzheimer's disease (AD), Parkinson's disease (PD), Convolutional Neural Networks (CNN), Recurrent Neural Network (RNN), Deep Learning (DL)

1. INTRODUCTION

ALZHEIMER's disease (AD) is one of the most prevalent neurological diseases with a significant growth rate in incidence [1]. The progression of AD gradually results in memory deterioration and impairment of cognitive functions, ultimately leading to irreversible neuron injury [2]. Alzheimer's disease (AD) is a complex progressive neurodegenerative disease that often occurs in people over 65 years old [3].

It affects human behavior, memory, and judgment. Because there is no cure for AD so far, many research works focus on how to effectively confirm the diagnosis of AD and start intervention as early as possible, which is also clinically meaningful. Functional magnetic resonance imaging (fMRI) is an emerging Neuro-imaging method that can characterize the structure and function of the nervous system. fMRI detects the brain's metabolic activities by measuring the changes in blood flow and blood oxygen concentration. fMRI plays an important role in the study of AD [4].

In previous research, the fMRI data were usually used to construct functional networks [5]. Graph theory and machine learning methods would be used to analyze the functional brain networks for figuring out the characteristics of AD [6].

Padilla et al. [7] introduced the early detection of Alzheimer's disease (AD) computer-aided diagnosis (CAD) technique on the basis of nonnegative matrix factor (NMF) and trustworthy vector machines (SVM). The CAD technique was designed to analyze and classify functional brain images.

For this reason, two separate brain image databases are chosen: a single-photon emission computed tomography (SPECT) and an image of Positrons emitting tomography (PET), each with reference data of Alzheimer's disease (AD) patients and health checkups. The most common approach in AD Neuro-imaging research has been the hierarchical design, where different areas of the brain/voice are automatically evaluated. Deep learning is used for data interpretation and analysis.

In addition, variations and data models can be classified. This allows for decisions that cannot usually be taken using standard processes of time saving and efforts [8]. fMRI is an effective imaging mode for assessing the interconnection of structurally separated and functionally different brain networks, especially in resting-state fMRI. The neural network which is the basis of the interactive pathogenesis can thus be established during the neural degenerative stages. AD can be diagnosed with fMRI data [9], [10]. AD recognition has been extended too many different methods focused on deep learning. Nevertheless, several controversial findings encouraged us to participate in the literature review to determine the current operating condition and what could be the potential innovations.
In this section, the primary study concern is if DL techniques have been able to classify AD using Neuro-imaging data. The training dataset scale is considered to significantly impact the classifier's output over an undefined test range [11].
In each dataset, the amount of AD and MCI topics can be minimal, inadequate for deep models to be evaluated. For multimodality experiments, the condition is worse. Any experiments, however, have mixed datasets. While it can result in more heterogeneity by integrating multiple datasets, this may advance a broad and stable classification and prediction model. Using data augmentation is another means of addressing the small number of topics in a dataset.
Data increase is a technique that increments the data range of training model applications without additional data being obtained. In approximately 20 percent of research aimed at enhancing classification performance, data enhancement strategies like random translation, rotation, reflection, adding noise, gamma filter, blurring, cutting, and scaling were used where appropriate [12].
Although no treatment has been proven to be effective in preventing the progression of AD [13], the early diagnosis of AD still remains important to subsequent treatments to delay the onset of cognitive symptoms [14]. Based on machine learning methods are developed to identify anatomical differences between Alzheimer's disease (AD) patients and normal controls (NC), and predict the progression of mild cognitive impairment (MCI) using structural magnetic resonance imaging (sMRI), which is sensitive to morphological changes caused by brain atrophy [15].

In recent years, deep learning methods have shown great success in image classification tasks such as medical imaging analysis. For instance, deep convolutional neural networks (CNNs) are empirically verified to have the excellent ability to learn high-level features from sMRI data, and greatly improve the performance of brain disease diagnosis with the efforts of many researchers [16].

RELATED WORK

In this section, we briefly introduce previous studies on computer-aided AD diagnosis methods with sMRI and fMRI data. Then we respectively review the multiple learning algorithm and statistical test mechanism related works in medical imaging analysis.

A. Alzheimer's Disease Detection with Smri

According to the partition of ROIs from sMRI scans, the previous brain disease diagnosis studies could be roughly divided into three categories, including voxel-level, region-level, and patch-level methods. The voxel-level methods [17]–[20] aimed at distinguishing disease-related microstructures in MR images of the patients and normal controls. In a voxel-wise manner, the tissue (e.g., gray matter and white matter) densities were generally measured as features for the classification algorithms.
However, only analyzing features on isolated voxels would lead to the ignorance of the high correlation between voxels. Another limitation of voxel-level methods was the over fitting problem, because the voxel-level feature representation always had a high dimensionality compared with the small number of subjects for model training.
Therefore, feature dimension reduction was the main challenge of voxel-level methods for improving the performance of AD classification. In [21], a fully convolutional network (FCN) was trained on the randomly sampled patches from the full MRI volumes. Based on the trained FCN, the voxels of high risk were selected and fed to the multilayer perceptron (MLP) for individual-level AD classification. However, the spatial correlations among patches were processed inadequately in these works.
A hierarchical full convolutional neural network was proposed for AD diagnosis [22], which could learn multi-scale feature representations (e.g., patch-level, region-level and subject-level) from sMRI scans. Then a pruning strategy was used to remove uninformative patches and cut down the learnable parameters.
However, it may lead to the loss of potential spatial correlation between the removed patches and left patches. Therefore, highlighting the discriminative features while retaining the spatial correlation among patches is still a challenge in patch-level methods.

B. Alzheimer's Disease Detection with fMRI

Disease Progression [23] Modeling (DPM) of Alzheimer's to show short-term clinical data on the long term pathologic trajectories. DPM has the ability to show an important clinical device for automatic diagnosis, together with the capacity to provide a data-driven description of the natural development of the disease through an explicit description of biomarker transitions from normal to pathological phases across the disease axis. Throughout this analysis, they had reformulated DPM in a probability system to quantification the diagnostic complexity of the seriousness of individual diseases with regards to missing metrics, biomarkers, and follow-up data in a hypothetical clinical scenario. They indicate that the step performed in 582 amyloid positive test entities is of high diagnostic reliability.

This measurement significantly minimizes the uncertainty of the forecast. The change from normal to pathologic stages is mainly related to increasing hypo-metabolism of the brain, temporal atrophy, and decreasing clinical levels. Recently suggested [24] an approach to the integration of global and local characteristics with the use of three-dimensional networking and structural analysis to diagnose AD from Hippocampus Analysis (HA). The proposed method can enhance classification with local visual and global formal features.

C. Multiple Learning Algorithm

The Deep Learning (DL) is a neural network that uses several variables and layers to define. There are a variety of simple network architectures [25], including CNNs, mainly a standard spatial mutual weight neural network [26].

The CNN is designed to identify images that see the edges of a known target on the image by making convolutions inside [27]. (ii) Recurrent neural networks are names of artificial neural networks where a graph is generated by specific associations between nodes in the temporal chain. RNNs can use their internal condition to handle the sequences of inputs, unlike feed-forward neural networks. RNN is meant to identify sequences such as a voice signal or a text [28], for example. (iii) In recursive neural networks, the input sequence does not include a time dimension, and the input must be hierarchically evaluated in a tree form [25, 27]. Various external inputs usually contribute to distinct brain functions, and various functional brain representations are displayed by different brain activities [28]. For that function, the classification of images plays an essential role in detecting various brain functions.

Several deep learning approaches have recently been suggested to carry out image recognition for various brain activities [29, 30]. The C3d-LSTM model consists of two basic deep learning model structures, namely a 3D convolutional neural network (CNN) [31] and a long short-term memory (LSTM) [32] network. The 3D CNN is a generalization of traditional CNNs on 3D images. The biggest change is the conversion of convolution kernels from 2D to 3D, which makes the model more suitable for extracting features from 3D images. Therefore, the 3D CNN can be used to handle the spatial structure information contained in the fMRI data. The LSTM network is an improved form of the traditional recurrent neural network (RNN) that can solve the gradient vanish problem of long-dependence in time series more effectively than RNNs [33]. It is often used in natural language processing and speech signal processing; through its internal complex gate structure, time-varying information and correlation information in time series data can be well characterized.

Although multiple learning algorithm and statistical test mechanism have good performance in the field of brain disorder diagnosis. To improve the performance metrics of the proposed classification model in terms of Sensitivity, Specificity and accuracy, we propose a hybrid learning methodology to deal with fMRI image sets using 3D – Convolutional Neural Network (3D – CNN) along with statistical test landmark parameters.

II. PROPOSED METHODOLOGY

The aim of this proposed work is to develop a method for deep learning training that did not require the removal of white and grey matter. This experiment's method is based on Faster R-CNN on the MATLAB platform, but it takes a long time to train and test.

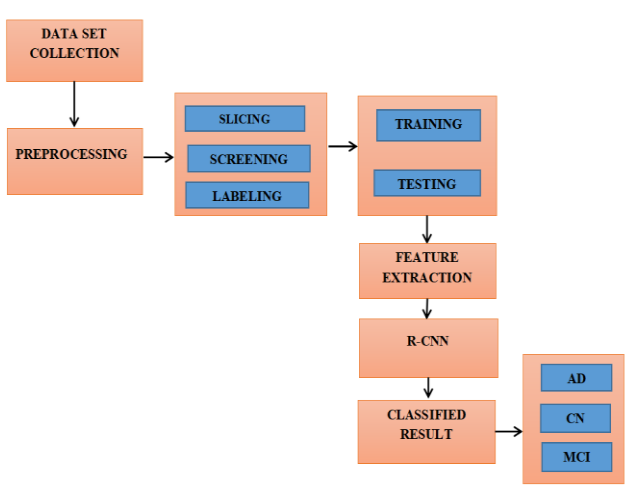

Figure 1: Block diagram of proposed method

1. Data Collection:

The Alzheimer's disease Neuroimaging Initiative (ADNI) is linked to experimental data to figure out how cognitive, clinical, biochemical, imaging, and genetic biomarkers, as well as early diagnosis and follow-up, are related to Alzheimer's. By utilizing novel diagnostic techniques at the earliest possible stage, ADNI is committed to detecting AD before dementia develops

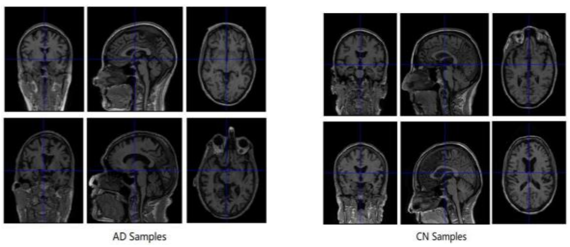

Figure 2: Different types of samples

All raw data are MRI images of patients' or volunteers' heads. The ADNI 1 data set is divided into three categories: Cognitively Normal (CN), Mild Cognitive Impairment (MCI), and Alzheimer's disease (AD). AD indicates that patients have been diagnosed with Alzheimer's disease, CN indicates normal cognitive status, and MCI indicates patients with mild cognitive impairment.

2. Dataset Preprocessing

To deal with 3D images like MRI, deep learning requires preprocessing of the initial data. This experiment's preprocessing of the data set consists of three steps: Slicing, screening, and labeling with an MRI. The MRI image is sliced (layered) from the bottom to the top of the head in slicing. Slicing is carried out with a piece of MATLAB code. A portion of the slice image is kept in Screening, and 100 samples were chosen for each category. A total of 3343 images were used as the data set following the screening, with approximately 10 slices chosen for each sample.

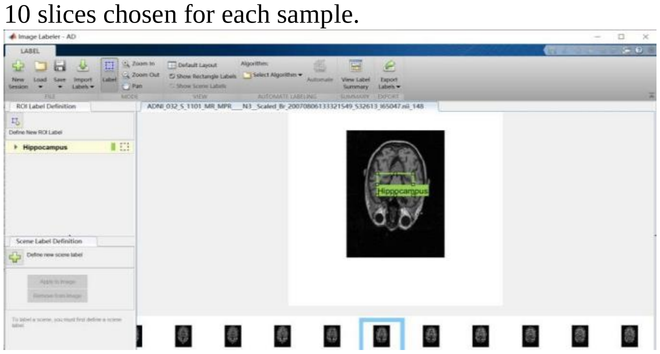

Figure 3: Labeling the sample data

One of MATLAB's useful data labeling tools is Image Labeler, which can be used to define rectangular ROI labels, scene labels, pixel ROI labels, and so on. In this experiment, Image Labeler is used to mark a rectangular ROI that contains the image's pons and hippocampus.

3. Training process:

The Faster R-CNN training process consists of four steps. The first is to train a Region Proposal Network (RPN), which initializes the feature extraction network and trains the RPN network using a pretrained model on the ImageNet data set. Using the GPU, the training process is carried out.

Faster R-CNN Object detector for AD, CN and MCI						
S. No	**Iteration**	**Time elapsed**	**Loss**	**Accuracy**	**RMSE**	**Learning rate**
1	50	00:00:00	0.0193	98	0.36	0.001
2	100	00:00:10	0.0035	97	0.26	0.001
3	150	00:00:19	0.0048	96	0.24	0.001
4	200	00:00:27	0.0031	95	0.34	0.001
5	250	00:00:36	0.0042	92	0.25	0.001
6	300	00:00:48	0.0056	91	0.28	0.001
7	350	00:00:54	0.0085	100	0.39	0.001
8	400	00:01:10	0.0013	92	0.45	0.001
9	450	00:01:16	0.0085	93	0.25	0.001
10	500	00:01:24	0.0075	89	0.26	0.001
11	550	00:01:34	0.0081	88	0.27	0.001

Table 1: First step of training with Faster R-CNN

The second step is to train a Faster R-CNN Network using the RPN from Step1.This step utilizes the model pre-trained based on Image Net to initialize the Fast R-CNN feature extraction network

Training a faster R-CNN network using Step 1						
S.No	**Iteration**	**Time elapsed**	**Loss**	**Accuracy**	**RMSE**	**Learning rate**
1	50	00:00:00	0.0193	95	0.36	0.001
2	100	00:00:20	0.0035	96	0.26	0.001
3	150	00:00:29	0.0048	96	0.24	0.001
4	200	00:00:34	0.0031	91	0.34	0.001
5	250	00:00:39	0.0042	82	0.25	0.001
6	300	00:00:52	0.0056	91	0.28	0.001
7	350	00:00:59	0.0085	100	0.39	0.001
8	400	00:01:14	0.0013	99	0.45	0.001
9	450	00:01:19	0.0085	94	0.25	0.001
10	500	00:01:29	0.0075	97	0.26	0.001
11	550	00:01:42	0.0081	99	0.27	0.001

Table 2: Second step of training with Faster R-CNN

Re-training RPN with Fast R- CNN and weight sharing is the third training step. We set the learning rate of the feature extraction network parameters shared by RPN and Fast R-CNN to 0. It uses the parameters of the Fast R-CNN network from Step 2 to initialize a new RPN network. It does this by fixing the feature extraction network and only learning the RPN network Parameters' characteristics. All common convolutional layers have been shared by both networks at this point

Training a faster R-CNN network using Step 1						
S.No	**Iteration**	**Time elapsed**	**Loss**	**Accuracy**	**RMSE**	**Learning rate**
1	50	00:00:00	0.0193	95	0.36	0.001
2	100	00:00:20	0.0035	96	0.26	0.001
3	150	00:00:29	0.0048	96	0.24	0.001
4	200	00:00:34	0.0031	91	0.34	0.001
5	250	00:00:39	0.0042	82	0.25	0.001
6	300	00:00:52	0.0056	91	0.28	0.001
7	350	00:00:59	0.0085	100	0.39	0.001
8	400	00:01:14	0.0013	99	0.45	0.001
9	450	00:01:19	0.0085	94	0.25	0.001
10	500	00:01:29	0.0075	97	0.26	0.001
11	550	00:01:42	0.0081	99	0.27	0.001

Table 3: Third step of training with Faster R-CNN

RESULT AND DISCUSSION

The raw fMRI image set pertaining to human heads that was downloaded from ADNI was imported into this experiment, and the required data set was generated following preprocessing. A Faster R-CNN-based AD detection model was constructed and compared. For feature extraction, MATLAB supports several basic networks.

Figure 4: Result of AlexNet+Faster R-CNN

According to our tests, the new Network and Faster R-CNN, which was adapted from the VGG16+Faster R-CNN network, is able to detect AD samples with a precision of 100 percent and an accuracy of 97.67 percent for the detected image.
The AlexNet + Faster R-CNN [36] fail to correctly classify AD samples and detect hippocampus region. The accuracy is only 62.1%. The GoogleNet+ Faster R-CNN fails to correct classification of the CN and MCI samples, the confidence of the bounding box contains the hippocampus region. The network

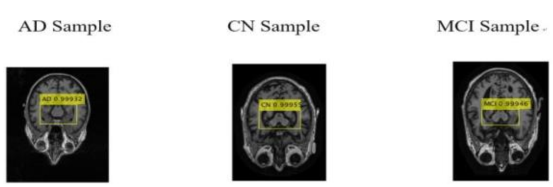

Figure 5: Result of 3-D CNN

structure is too deep, the amount of calculation increases, the detection time for the entire validation set. This proposed work modules tested with help of ADNI data with nearly 2016 samples to classify the fMRI images into Alzheimer's disease, Mild Cognitive impairment and Normal Cognitive categories. That too diagnosis of Alzheimer's disease, Mild Cognitive impairment in the early stage images has been detected and classified with accuracy of 98.6% under the parameter evaluation of area under curve, specificity and sensitivity. The future work will be carried over with the help of 4D- CNN on both structural and functional fMRI images in order to have better studies on voxel based morphometric and activity of the brain.

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