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Diagnosis of Parkinson’s Disease using Deep Learning Network

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ABSTRACT

Early-stage diagnosis of Parkinson’s Disease (PD) is still a challenging task to the neurologists. An effective system is used for volume-based slices of Single Photon Emission Computed Tomography (SPECT) image to diagnose early PD. 16 slices which has significant region of interest are taken out from the SPECT images which is called as two-dimensional volume-based slices (2Dvs) for the analysis. The normalization technique called bilateral filter is used to enhance the Striatum of 2Dvs which make the architecture simpler. A deep learning technique called modified VGG16 architecture is used as a neural network to learn significant features from 2Dvs which could be able to discriminate Early PD from healthy control (HC). The architecture offers highest accuracy for discriminating Early PD from HC based on 10 cross fold validation. These techniques are practiced to develop a promising diagnostic model for early diagnosis of PD.

KEYWORDS: *SPECT, Early PD, VGG 16, Deep learning*

I. INTRODUCTION

PD is a movement disorder,causes due to deterioration of dopamine content in the striatum region of theSubstantia Nigra (SN). The PD is clinically recognizedby the cardinal symptoms like resting tremor, rigidity, postural instability, and bradykinesia, cognitive and psychiatric disturbances and it has an effective response to the drug levodopa (medication used to treat PD) in the advanced stage.However, thesesymptoms are unknown and ineffective response to levodopa at an early stage of the disorder[1, 2].

The SPECTimages are used forthe proper identification of PD. The procedure to take SPECT images are: The radiopharmaceutical drugis injected into the human body and it binds to the dopamine transporters in the striatum. The distribution of the drug in the brain locates the dopamine content in it [3]. Hence the quantification of dopamine content in the human brain found to be an appropriate biomarker fordiagnosing PD.The GE health care report [4] states that the normal SPECT scan has high striatal uptake (dopamine), which forms symmetric shape or two commashaped focal regions. Whereas an abnormal scan has reduced striatal uptake or circular region in one of the striatum, forming asymmetric shape. Changes in the shape of striatum is clearly identified by the image processing techniques [5,6].

The significant image processing techniqueis an intensitynormalization approacheswhich is to rectify the errors that arise due to physiological reasons and baseline calibration of a gamma camera.Theintegral and Cube based intensity normalization [7, 8, 9] approaches computethe mean integral value and cumulative intensity values of the image pixels by setting reference region outside the striatum. In another method,the normalization is done based on the maximum intensity value of the voxels, which may lead to wrong normalization because of peak intensity values due to noise.The bilateral filter calculates the weighted sum of nearby pixel values. The weight of the pixels basically depends on both the spatial and the intensity distance of the pixels. The noise of the nearby pixels is averaged to preserve the edges of the images well [10].

The analysis of 2D image and averaging image slices are the initial stage of early PD diagnostic process and it must be improved [11]. In addition to that, voxel (3D view of pixels) based analysis [12, 13] was also carried out, where the voxels are treated as features. The voxels are ranked based on its significance and top most features are taken for the analysis to diagnose Parkinson's disease.Voxel based analyses are found to be very tough for clinical practices [14]. Hence, the CAD system is involved to quantify the features of volume based image slices [15], which may comprehendthe specific uptake pattern during the normal and diseased state.

The machine learning techniques play a major role in medical image analysis to diagnose the disease. In particular, deep learning algorithm is a significant tool in learning the features directly for image classification. It is highly accurate system than machine learning because it learns the features directly than extracting features from hand designed manner. Recently, Convolutional Neural Networks (CNNs) is a powerful tool for analyzing medical images especially SPECT image to diagnose PD [16].

Bounding box technique was implemented on regions of interest (ROI) by calculating the intensity threshold. The rest of the regions are removed. The performance metric of the network is evaluated by10-fold cross-validation. Another deep learning network called PDNet is designed for PD classification. [17]. In their study, the system was trained on SPECT images obtained from PPMI and it shows a high accuracy. Though the system is more accurate, it is complex to implement and time consuming. The practical implementation of such network solutions is not feasible, as time is of crucial importance in the diagnosis of PD. To overcome this issue an efficient CNN is developed to classify Early PD from HC which offers a high-performance metric in terms of accuracy.

This paper organizes as follows. Section 2 contains the methods used like bilateral filter, The proposed network structure (modified VGG16). Section 3 describes the results and related discussions. Finally, conclusions are drawn.

II. METHODS AND MATERIALS

The Dataset Used

The SPECT images are taken from the international PPMI database for the analysis. The hybrid ordered subset expectation maximization (HOSEM) algorithm, Iterative reconstruction, Attenuation correction has applied for processing the raw SPECT images. The details of the dataset used for the analysis are given in Table.1. The mentioned SPECT images are enhanced by bilateral filter and the images are trained by the proposed network. Fig. 1 illustrate the 2Dvs for early PD and HC.

Table. 1 Details of input dataset

Categories	Features
Total number of images	700
No. of classes	2
Data type	Image
Size of the image	224, 224, 3

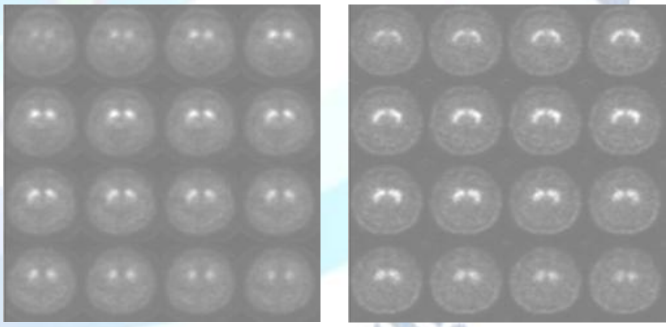

Fig. 1 Two-dimensional volume-based image slices chosen from the SPECT (a) early PD (b) HC

The Modified VGG 16 Network Architecture

The overall flow of the proposed work is clearly explained in Fig.2.The 2Dvs are preprocessed using bilateral filter. The preprocessed image slices are given to the CNN architecture in order to make the network much simpler. The proposed network is a modified version of VGG 16. The network consists of four convolution layers and two dense layers for discriminating early PD from HC.

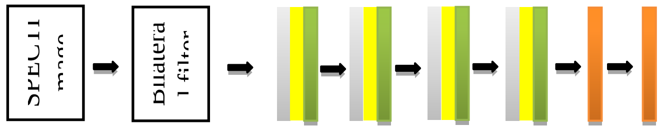

Fig.2 Overall Workflow of the Proposed Work

VGG 16 is one of the best deep neural networks that has been employed for image classification tasks. The network consists of 13 convolutional layers, five max pooling layer and three dense layers with the uniform kernel sizes like 3x3 as shown in Fig. 3. However, one of the main drawbacks of the network is overlapping pixel blocks, which leads to an increase of memory consumption for learning the features of image.

On contrary, the proposed modified VGG 16 networks have only four convolutional layers and three dense layers, each with a kernel size of 3 × 3. The uniform kernel size is taken for the network which leads to much better feature learning with least number of training parameters. These smaller sized kernel gives lower costs due to less number layers than larger sized kernel. Though the multiple number of larger sized kernels provide more in-depth network architecture which is time-consuming and not feasible for medical applications. Therefore, by reducing the kernel size, the proposed network gains the advantage of learning the features from the image faster. Furthermore, the proposed network is more robust and performs better than VGG 16 with admirable accuracy, sensitivity, and specificity (Fig.5).The ReLU (Rectified Linear Unit)activation function allows faster training of CNN, since the calculation of its derivative has a lower computational cost, without losing any of its generalization ability [18].

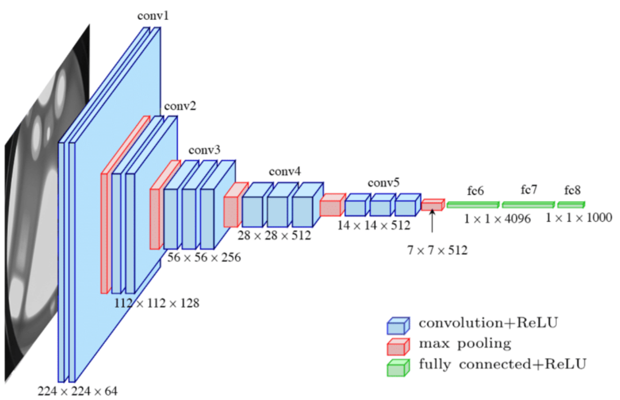

Fig.3 Pretrained network of VGG16 [19]

The ReLU itself is a non-saturating activation function and is defined by

$f(x) = x^{+} = max(0, x)$ (1)

where x is the input to a neuron.The image normalization process is done by bilateral filter which described below. In addition, our network only utilizes the ReLU activation function in all three layers. The proposed network model is optimized using the stochastic gradient descent with momentum optimizer (sgdm) with the learning rate of 0.01. These standard parameters of sgdm have been proven for neural networks to be computationally efficient, little memory usage and well suited for problems with big data. Hence these parameters are utilized in the proposed network. The input images utilized to train the network are resized from the original size of 522× 529 x 3 to 224 × 224 x 3. Since this paper is focused on the classification between early PD patients and HC, i.e., a binary classification problem.In the architecture112 nodesare used in each of our layers. Dropouts are used in the proposed work to avoid overfitting of data which will also improves the performance of the network.

Image preprocessing

The preprocessing technique is used to highlight the region of interest (ROI) in an image. The bilateral filter is implemented for SPECT images in order to enhance the edges of the striatum region to diagnose Early PD. It calculates the weighted sum of nearby pixel values. The weight of the pixels basically depends on both the spatial and the intensity distance of the pixels. The noise of the nearby pixels is averaged to preserve the edges of the images well. The basic mathematical equation of the bilateral filter is given in following equation.

$$\widetilde{I(x)} = \frac{1}{C}\sum_{y\in N(x)} e^{\left(\frac{(X^2-Y^2)}{2*\sigma\_d^2}\right)} e^{\left(\frac{-I(X^2-Y^2)}{2*\sigma\_r^2}\right)} (1)$$

Where, **σ**_d &**σ**_r – Parameter that controls weights of spatial and intensity domain. The preprocessed 2Dvs image slices are shown in Fig. 4. It shows the deviation between PD and HC.

Training and Testing the Network

A modified VGG 16 is trained and tested using the 500 SPECT images for both early PD and HC. The augmentation process is not done for identification of the PD in the early stage. The 10-fold cross validation is accomplished to evaluate the performance of the modified VGG 16. It consists of 10 subset of data which includes PD and HC. The dataset is divided equally for the subset. One subset is used for testing and the remaining subset is used for training the network. The evaluation metrics of the network is calculated from the confusion matrix and it is given as

$$\text{Accuracy} = \frac{TruePositive\ (TP)+TrueNegative\ \ (TN)}{TruePositive\ (TP)+TrueNegative\ (TN)+ FalsePositive\ (FP)+FalseNegative\ (FN)}$$

$$\text{Sensitivity} = \frac{TP}{TP+FN}$$

$$\text{Specificity} = \frac{TN}{FP+TN}$$

III. RESULTS AND DISCUSSION

Preprocessing using Bilateral Filter

The extracted sixteen slices are normalized using bilateral filter to enhance the edges of the striatum region alone for the subsequent analysis.Fig. 4 shows the normalized image slices of early PD and HC. It is evident from the Fig. 4 that PD has reduced comma shaped striatum and the HC has comma shaped striatum. The preprocessing technique increase the focus on the striatum which also increases the diagnostic accuracy and reduces the computational cost. Hence the classification takes the important role to discriminate early PD and HC. These enhanced images are given to the network for learning the features of the images.

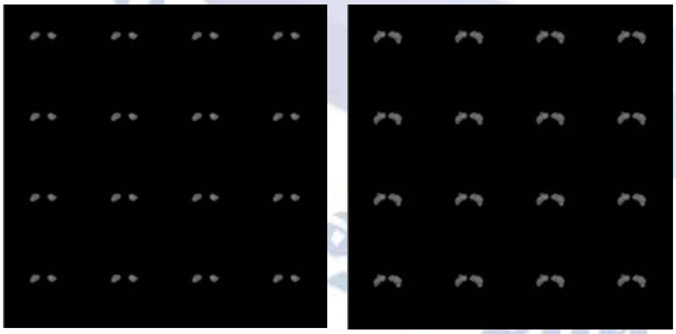

Fig. 4 Enhanced image for (a) early PD, and (b) HC

Network Performance

The enhanced2Dvs are given to the modified VGG 16 networks. The network has designed in such a way that it provides highest performance and less computational cost. The network parameters are given in the Table.2.These parameters are selected by design calculation of the network. Using the given parameter, the network is trained by the 2Dvs SPECT image slices to diagnose early PD.

Table. 2. The parameters of the proposed network

S. No.	Network Parameters	Numeric value
1	Image size	224,224,3
	Convolution	
2	No. of filters	32
3	Kernel size	3x3
4	Stride	1,1
5	Padding	same
	Max. Pooling	
6	Kernel size	3x3
7	Stride	2,2
8	Padding	0
9	Output size	2
10	Dropout	50%

The enhanced images are given to the network for training it appropriately. The ten fold cross validation method is executed to evaluate the performance of the network to overcome the variability in the classification. 50% dropouts also minimize the overfitting of data which in turn improves the classification accuracy. Table 3. Illustrates that the classification task converged quickly and achieved appreciated diagnostic accuracy of 95.90%, sensitivity of 94.39%, specificity of91.37%. The performance metricsconfirm that the proposed network offers high probability of diagnosing early PD when compared with the pretrained neural network (VGG 16).It elucidatesclearly that the modified VGG 16 network offers appreciated output in discriminating early PD from HC.

Table. 3. Performance Metrics of the Proposed Neural Network

Folds	Training Accuracy (%)	Testing accuracy (%)	Sensitivity (%)	Specificity (%)	Pretrained Network (%)
1	92.35	94.87	97.87	93.87	92.01
2	90.15	98.78	94.17	94.94	90.32
3	95.45	97.77	91.26	80.00	93.56
4	96.70	96.00	94.00	91.18	91.78
5	93.55	96.87	95.73	92.38	95.54
6	94.54	94.99	97.00	86.49	94.25
7	96.25	95.99	94.75	100.00	90.21
8	91.98	95.98	92.26	95.00	93.45
9	95.25	91.88	93.21	89.47	91.02
10	92.74	95.89	93.65	90.32	90.25
	93.90	**95.90**	**94.39**	**91.37**	**92.23**

IV. CONCLUSION

An early diagnosis of Parkinson's Disease (PD) is made easy using a recent technology called Convolutional neural network. The two-dimensional volume based slices (2Dvs) are extracted from the SPECT images based on the high striatal uptake region. The edges of the 2Dvs are enhanced using bilateral filter. The enhanced 2Dvs is subjected to the modified VGG 16 to enrich the diagnostic accuracy to reduce the rate of misclassification between PD and HC. The network uses reduced number of layers and optimal parameter to reduce the computational cost and to use minimum memory. The network offers high diagnostic accuracy of 95.90%, sensitivity of 94.39%, Specificity of 91.37%. Hence the proposed system aids the clinicians to diagnose PD in earlier stage.

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