PARKINSON DISEASE DETECTION USING DEEP LEARNING

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ABSTRACT

Parkinson's disease (PD) is a long-term degenerative disorder of the central nervous system that mainly affects the motor system. The symptoms generally come on slowly over time. Since it is related to the brain abnormality, electroencephalogram (EEG) signals are usually considered for the early diagnosis. Many other symptoms like small handwriting, vocal impairment, loss of smell, masked face, etc can also be used for its detection. In this work, the data from Parkinson's Progression Markers Initiative (PPMI) database was obtained based on one of these symptoms. PPMI is an observational, multicentre study that collects clinical and imaging data and biologic samples from various cohorts that can be used by researchers to establish markers of disease progression in PD. In this project, we proposed Neural Networks based model which aims to help doctors and people in diagnosing Parkinson Disease in early stages. One of the neural networks we decided to use is Convolutional Neural Networks (CNNs) which have been established as a powerful class of models. We have tried to create a system that will help in automatically diagnosing Parkinson Disease based on the medical imaging results plus the voice data of the patient available to us.

INTRODUCTION

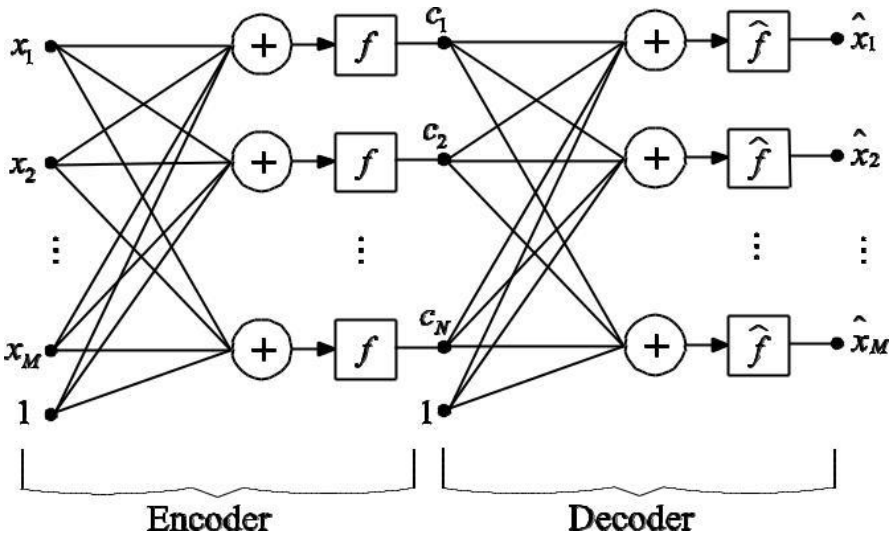
Parkinson Disease is a neurological degenerative disorder that affects the working of central nervous system and hence affects are seen physically on the body. The number of neurons in the human mind is maximum during the time of birth. Neurons don't have the ability to grow as the older we get, the neurons start dieing out and are irreplaceable. This is the main cause behind the Parkinson Disease. Neurons produce a chemical fluid Dopamine, which is solely responsible for the movement in the body and transmission of signals amongst the neurons. As the Dopamine levels starts dropping with age, our neurological condition starts slowing down, influenced by the various communication modes in the brain. These affects incur very slowly, hence are usually not visible until the patient's condition has worsened. Some of its symptoms are loss of balance, slow movements and unstable posture.

WHO records show that this disease has affected almost 10 million people around the globe. Patients aren't diagnosed of it in early stage, resulting in untreatable permanent neurological disorder. In study, we aim to develop a deep learning model implementing CNN (Convulational Neural Networks) for the objective diagnosis of Parkinson Disease in its early stages. Recent introduction of Neural Networks has changed level of the scientific and industrial researches and it has been applied to medical images for segmentation, lesion-detection, and disease classification. It has drastically improved the detection of various neurological diseases like epilepsy, schizophrenia, Alzheimer's etc. In our study we are planning to use decisive features like like voice impairment, dopamine transporter imaging, FP-SPECT imaging, and olfactory loss decided over the course of time for the prediction of Parkinson at an early stage and the dataset featured in the study is taken from Parkinson's Progression Markers Initiative (PPMI) database.

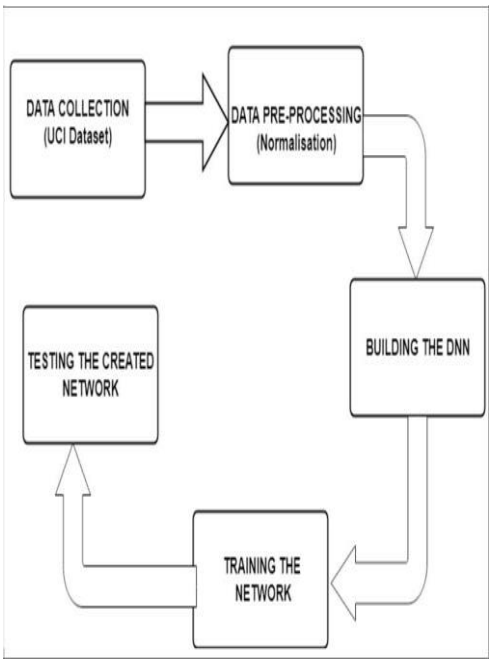
HYPOTHESES AND PREDICTIONS

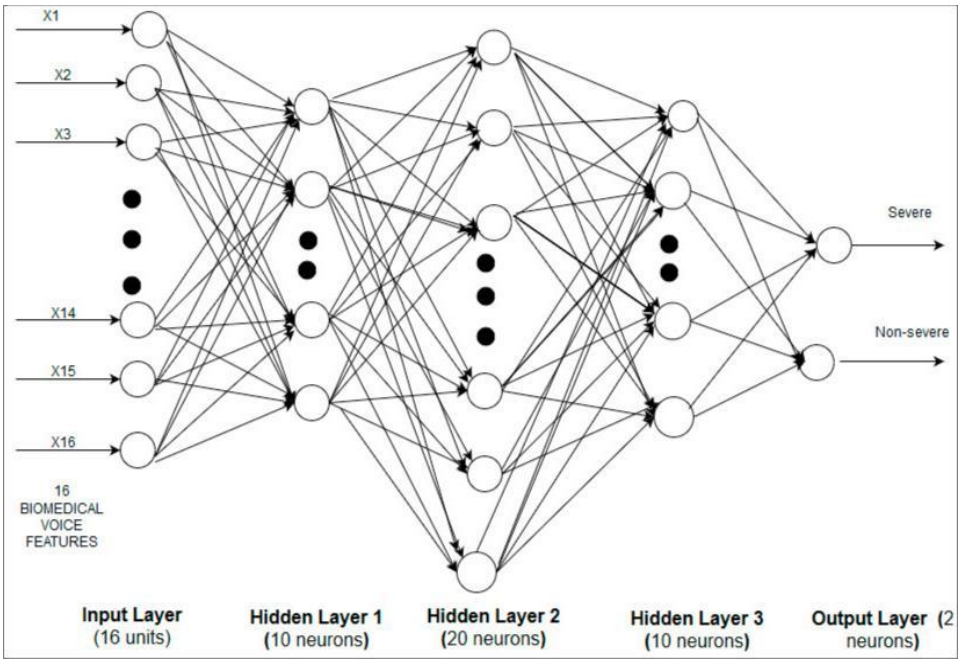
90% of Parkinson patients have vocal impairment and speech problems which are one of the earliest indicator of PD. Patient's voice tends to stutter and progressively becomes affected as the disease becomes more severe. We have mentioned nine papers regarding this symptom.

Research Paper [1] has used deep neural network on dataset of voices. First, the speech signals are filtered to eliminate noises and segmented with time-windows. From each segment, several features are extracted during the second step. Third step is classification. DNN uses Stacked Auto Encoders (sAE) to reduce the dimension of the features and classifies the samples by the "softmax layer". In this research, sAE contains two encoder part of the trained AE. Limited Memory BFGS optimization algorithm is one of the most suitable optimization algorithm employed for training of the DNN. This paper has compared the DNN classifier with SVM, DT and NB on two data sets: One is Oxford Parkinson's Disease Detection (OPD) database (195 samples 23 attributes) and the other is Parkinson Speech Dataset with Multiple Types of Sound Recordings (PSD) (1208 samples 26 attributes) obtained from Data Mining Repository of the University of California, Irvine (UCI) and hence results have shown better accuracy from DNN.



In the Research Paper [2], deep learning is used to analyze voice data of the patient to classify it into “severe” and “not severe” classes. This work is based on Parkinsons Telemonitoring Voice Data Set from UCI Machine Learning Repository. The various attributes of the data are subject number, subject age, subject gender, time interval, Motor UPDRS, Total UPDRS and 16 biomedical voice measures (features). The dataset contains 5,875 voice recordings of these patients. Then the collected data is normalized using min-max normalization and split the normalized dataset into parts of 80% (for train dataset) and 20%(for test dataset) for both motor UPDRS score and total UPDRS score. Input data has been fed into the training model with the help of lambda function. In the next step, DNN Classifier has been built using TensorFlow with Keras as the backend. The neural network contains 16 units (no. of inputs) in the Input layer, 10, 20, 10 neurons in each of the 3 hidden layers respectively. The network was further trained with 1000 and 2000 steps respectively. The output layer contains two neurons corresponds to the two classes – “severe” and “non-severe”. The evaluation metrics used in this research are the two UPDRS (Unified Parkinson’s Disease Rating Scale) scores - total UPDRS (Accuracy is 94.4422% and 62.7335% for train and test dataset) and motor UPDRS scores (Accuracy is 83.367% and 81.6667% for train and test dataset). This paper has also compared the results with Nilashiet al.



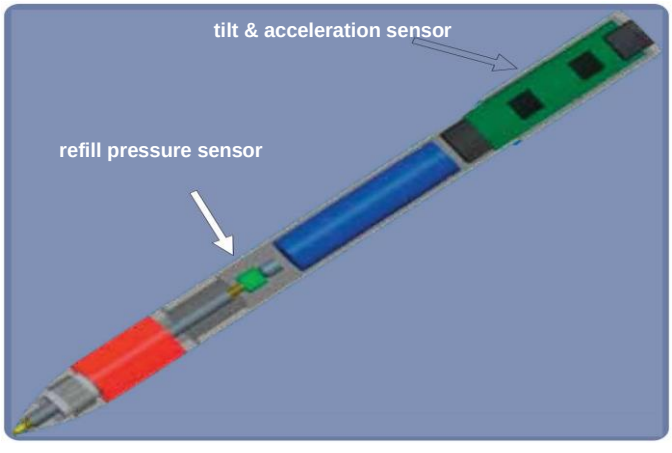


In the Research Paper [3] an attempt has been made to check the improvement in the accuracy while classifying the PD group from the healthy control group by using nonlinear feature selection algorithm with different feature sets such as the original feature sets (OFS) as well as the PCA based feature sets. The Dataset used in this paper has been taken from Max little University Oxford, in collaboration with the National Centre for Voice and Speech, Denver, Colorado. The original data collected from the dataset composed of voice measurements from 31 people out of which 23 were diagnosed with PD. PCA is applied on the original dataset to compress the data and to extract important information. Authors have used nonlinear classifier with decision tree for classification of groups are as follows RPART, C4.5, PART, Bagging classification and Regression tree (Bagging CART), Random Forest and Boosted C5.0. The parameters used to compare the performance and validations of classifier are accuracy, sensitivity, specificity, positive predictive value (ppv), negative predictive value (npv). In this paper it can be seen that Random forest performs better with PCA based feature sets in terms of accuracy among all the classifiers. It shows the maximum accuracy of 96.83%, maximum sensitivity of 0.9975 and also the maximum specificity of 0.9985.

Most works make use of audio-based datasets to cope with PD identification. The writing abilities are also affected by Parkinson Disease as the writing of parkinsonian patients is often distorted and smaller (micro-graphing) than that of healthy individuals due to the tremors, reduced movement amplitudes, slowness and rigidity.

In Research Paper [4], the former HandPD dataset was collected at the Faculty of Medicine of Botucatu, Sao Paulo State University, Brazil, being composed of images extracted from handwriting exams of individuals of healthy people and PD patients. This paper proposed a

learning of pen-based features by means of a Convolutional Neural Network (CNN), which can process information through a set of layers. Also this study extended the original HandPD dataset with signals extracted from the smart pen. The idea was the filling of form, containing some specific tasks that are supposed nontrivial to PD patients, such as drawing "spirals", "meanders", and performing the diadochokinese test. The signals generated though these movements are recorded by the pen. These signals concern six sensors i.e. Microphone, Fingergrip, Axial Pressure of ink Refill, Tilt and Acceleration in "X direction", Tilt and Acceleration in "Y direction"; and Tilt and Acceleration "Z direction". Since each sensor outputs the whole signal acquired during the exam, they represented this data as a time series. They divided the experiments into two datasets i.e. the meanders and the spirals. Both datasets are composed of 308 images, being 224 PD patients and 84 control group samples. In addition, they evaluated the robustness of CNNs over two different image resolutions: 64 × 64 and 128 × 128 pixels. Also, they evaluated the influence of the training set size over two distinct experiments: one with 75% of the dataset for training and 25% for testing, and another with 50% for training and 50% for testing purposes. In regard to the source-code, they used the well-known Caffe library5, which is developed under GPGPU (General-Purpose computing on Graphics Processor Units) platform, thus providing more efficient implementations. Each experiment was evaluated by a different CNN architecture i.e. ImageNet, Cifar-10, LeNet with different convolutional layers, pooling layers, normalization layer and activation functions, provided by Caffe using 10, 000 training iterations with mini-batches of size 16. In order to provide a statistical analysis by means of Wilcoxon signed-rank test with significance of 0.05, the study conducted a cross-validation with 20 running.

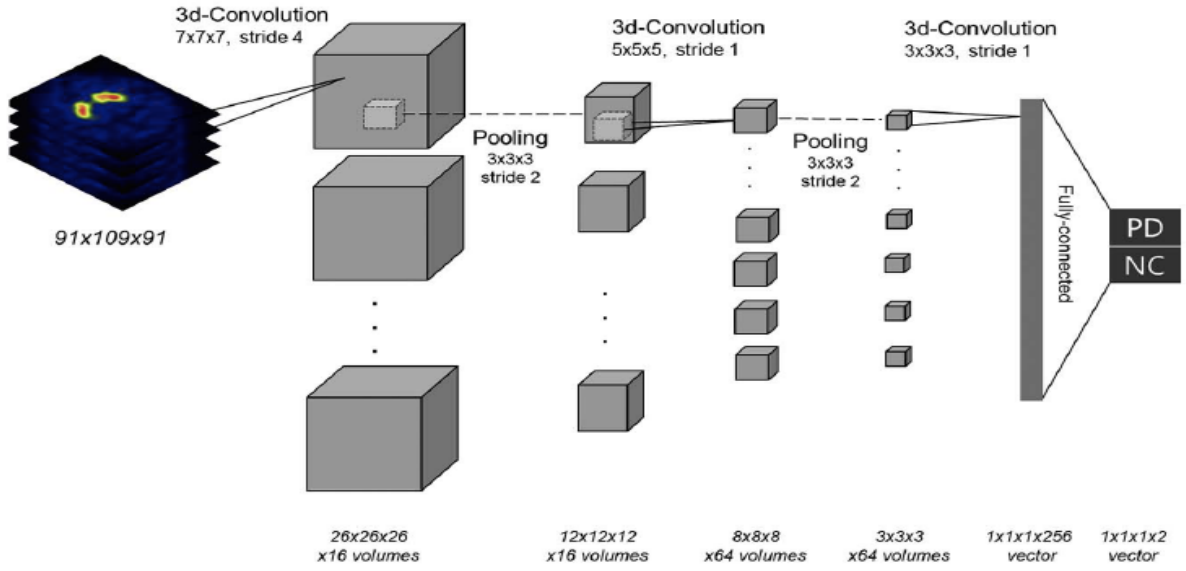


It can be observed that CNN-based features for meander dataset obtained the most accurate results for all experiments, except for the 75%−25% experiment with 64 × 64 images. Also, the best results were obtained by ImageNet architecture with 128×128 images and using 75% of the dataset for training purposes. The most accurate result for spirals dataset is 83.77% which was obtained by OPF with 64×64 images using 50% of the dataset for training purposes. The best results concerning CNNs were obtained using 75% for the training set. Since LeNet is shallower than ImageNet and CIFAR-10 architectures, it obtained the lowest accuracy recognition rates for both. The paper has also presented the accuracy results per class for both spirals and meander.

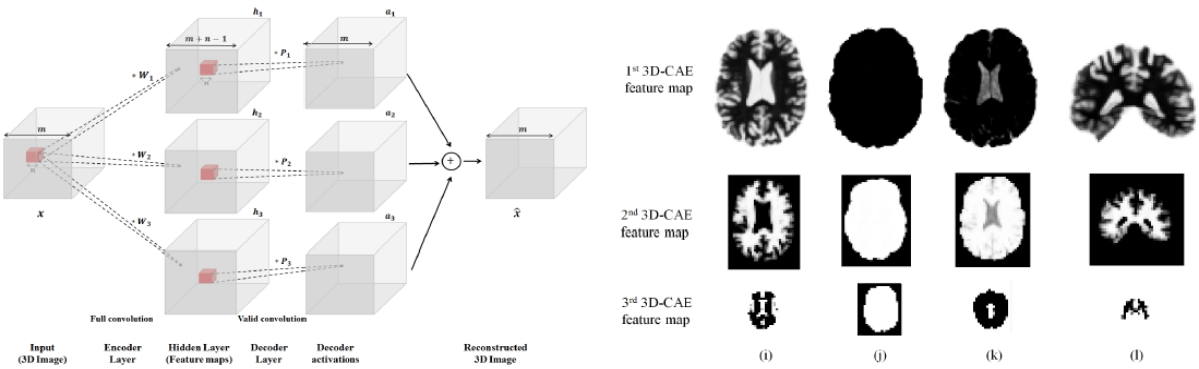
Another symptom i.e. Dopaminergic degeneration is a pathologic hallmark of Parkinson's disease (PD), which can be assessed by dopamine transporter imaging such as FP-CIT SPECT. Dopamine transporter (DAT) imaging such as 123I-fluoropropylcarbomethoxyiodophenylnortropane (FP-CIT) single-photon emission computed tomography (SPECT) is one of the established tools for the diagnosis of Parkinson's disease (PD). SWEDD (absence of imaging abnormality in patients) patients are approximately 10–15% of clinically diagnosed PD patients.

In the Research Paper [5], the aim is to develop an automated FP-CIT SPECT interpretation system based on deep learning for the objective diagnosis. In this study, the system was developed using Parkinson's Progression Markers Initiative (PPMI) database. The subjects of the PPMI cohort consisted of 431 patients with PD, 193 normal controls (NCs) and 77 patients with SWEDD. SPECT data were acquired into a 128 × 128 matrix. Input data were SPECT images downloaded from the PPMI database without and input values of voxels were rescaled by the range from 0 to 255, and then mean scalar value of each SPECT volume was

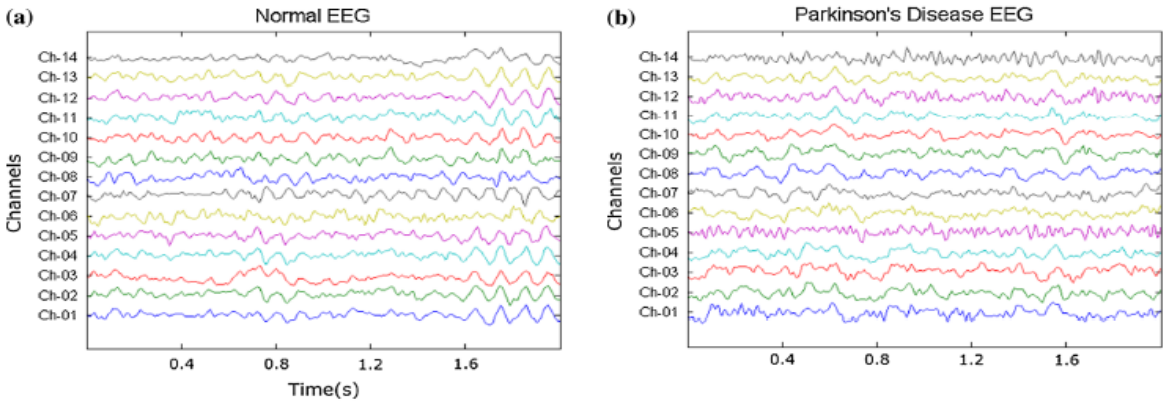
subtracted. After this step, each 3D volume (91 × 109 ×91) was used for input argument of PD Net. The images were passed by the 3-D convolutional layer which produced 16 feature maps after the 7× 7× 7 convolutional filters. As a stride size of four voxels was applied, size of the feature maps was 26 ×26 × 26. After the convolutional layer, Rectified Linear Unit (ReLU) activation layer and max-pooling layer were followed. 3-D convolutional layers with filter size of 5× 5× 5 and 3× 3× 3 were followed.



Consequently, these multiple layers produced 256 feature vectors which were connected to two output labels, Parkinson's disease and NC. A softmax function, exponential activation function with normalized operator, was applied to discriminate two labels after the output obtained. This network was trained to minimize the cross entropy loss between the predicted diagnosis and the true diagnosis of the patients.



PD is characterized by the gradual degradation of motor function in the brain. Since it is related to the brain abnormality, electroencephalogram (EEG) signals are usually considered for the early diagnosis. An automated detection system for Parkinson's disease (PD) employing the Convolutional Neural Network (CNN) using EEG signals has been proposed firstly in the Research Paper [6]. In this work, EEG signals of twenty PD and twenty normal subjects have been used. When the EEG signal displays complexity, aggravation of the PD is observed. This is due to the nonlinear components present in the EEG signals. Hence, it can be noted that the employment of nonlinear features extraction techniques would be useful in the differentiation of normal and PD EEG signals. Research has implemented a novel thirteen-layer deep CNN to characterize the two classes (PD and normal). The basic layers of the CNN include the convolution, max pooling, and fully connected (dense) layer. Adam optimization with a learning rate of 0.0001 has been used, along with activation functions like Relu for all layers and softmax for the last layer.



The dropout is set to 0.5 for dropout layer. All the EEG signals were subjected to the proposed CNN model which has been designed in Python language using Keras and was executed on a computer with a system configuration of two Intel Xeon 2.40 GHz (E5620) processors with a 24 GB random access memory. The proposed CNN model yielded an

accuracy of 88.25%, sensitivity, and specificity of 84.71% and 91.77%, respectively. The model has been validated with a stratified tenfold cross validation technique.

However, people are mostly familiar with the motor symptoms of Parkinson' disease, but an increasing amount of research is being done to predict the Parkinson's disease from non-motor symptoms that precede the motor ones. Non-motor symptoms are Rapid Eye Movement (REM), Sleep Behaviour Disorder (RBD) and Olfactory Loss. In the Research Paper [7] non-motor features has been used and the data from Parkinson's Progression Markers Initiative (PPMI) database has been obtained. Olfactory dysfunction acts as sensitive and early marker for Parkinson's disease. Olfactory dysfunction are in various forms for instance it may be impairment in odour detection or odour differentiation. Also, people suffering from RBD have disturbances in sleep including vivid, aggressive or action packed dreams. The REM Sleep Behaviour Disorder Screening Questionnaire has also been used. Cerebrospinal fluid is a clear, colorless body fluid found in the brain. Due to the close proximity with the brain, any protein or peptide which is related to the brain specific functionalities or disease are diffused into CSF. Hence, the CSF can act as an important biomarker for Parkinson's disease. Research has used automated diagnostic models using Multilayer Perceptron, BayesNet, Random Forest and Boosted Logistic Regression. It has been observed that Boosted Logistic Regression provides the best performance with an impressive accuracy of 97.159 % and the area under the ROC curve was 98.9%. Thus, it is concluded that this models can be used for early prediction of Parkinson's disease.

Focusing on symptoms and features of Parkinson Disease, we have studied Research Paper [8] which has used the neuro-imaging techniques *viz* fMRI, PET, etc. (non invasive methods) and invasive electroencephalography (invasive) methods that are applied for the diagnosis of

disease state. Functional magnetic resonance imaging (fMRI), is a non invasive method, has proven useful for studying the behavior (neural activity) of human brain through functional brain network analysis of the generated images. fMRI primarily, measures the hemodynamic

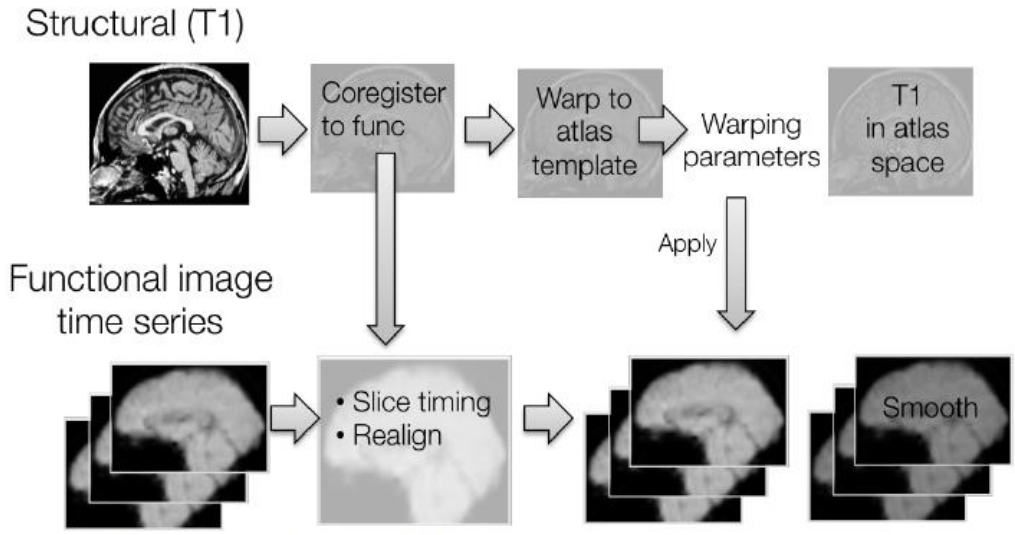
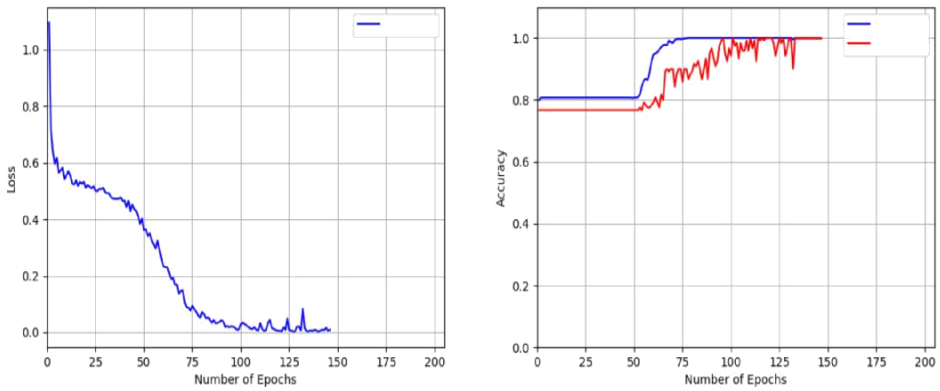


Figure 17.1. An illustration of the pre-processing steps performed on fMRI data.

response which is a reflection of the blood oxygenation level and the current locations can be used to decipher how the brain responds to various stimuli . Extracted features from this study are Aplitude of Low Frequency Fluctuations (ALFF), Fractional ALFF (fALFF), Regional Homogeneity (ReHo) and Functional Connectivity. The t-tests performed on ALFF, fALFF and ReHo feature maps for control group and PD group for show the different regions activated in the two groups, with trend of more activity in the PD patients. The regions in red hold the highest numerical values for the corresponding feature mapped, followed by yellow, light green and blue-green in decreasing order of values.

And lastly in the research paper [9], a deep learning model was proposed for classification and regression of PD diagnosis based on MR-Images and personal parameters i.e. (age, gender). A set of 3-D brain MRI images is used for PD diagnosis .PPMI provided the dataset

for this research. In the preprocessing stage, skull-stripping played an important part, in this technique removal of non-cerebral tissues (skull, scalp, dura) is done, Brain Extraction Technique helped in achieving that. After the reduction of images from skull stripping, led to reduction of images to 80x100x108 with the factor of 4.61. To make the accuracy of model better it was needed to feed large amount of data to model, for that data augmentation was used. In the skull stripped results, left half and right half are flipped to produce new data by keeping other things constant. A convolutional model was proposed having 2-conv layers followed by 1-max pooling layers repeated three times. The model was completed by making a fully connected layer and the final output layer. Soft max classifier was used in the output layer with cross entropy loss function. After each conv layer a normalization layer was introduced as well, with purpose to reduce the training time. Also the final connected layer was experimented with the introduction of age and gender of the patients which resulted a little bit of betterment of accuracy of the model. After the introduction of dropout layer in the penultimate layers the model achieved better accuracy, with further playing around with the regularization coefficients and keep probability the model was able to achieve 100% accuracy on all the test, train and validation set. Their study was able to show that Basal Ganglia and Substantia Nigra were already the main part in PD detection plus Superior Parietal part on right hemisphere of the brain is also very critical in diagnosis of Parkinson.



METHODOLGY AND EXPERIMENTAL DESIGN

According to the current availability of datasets from different sources, we have decided to use datasets which will be based on the MRI scans, biospecimen samples of PD patients, Biomarkers in Cerebrospinal Fluids imaging, SPECT images available from PPMI data collection repository or the Voice samples available from the UCI data collection repository.

For the pre-processing of the dataset we want to propose a fully connected convolutional network for which will have approx 4-6 convolutional layers, as per the results we will try to increase the layers and try to play around the hyper parameters. To perform this task we need a lot of computation power and time to train our model, but to reduce both these factors to a minimal certainty we decided to do reduction of the redundant or useless data and features using PCA or auto encoders (chosen on the basis of better results).

The main task of the whole project is making the data good enough to achieve good results. All the MRI results are available in DCM format (Digital Imaging and Communications in Medicine), therefore we first need to process these images in the suitable format, and store the pixel values after the choosing the proper axis of all the images one by one. And if we use the second dataset, we first need to check for a way to remove the class imbalance created by the over powered presence of Parkinson affected patients, after we need to process the files available in WMA format. We have decided to use the spectrogram formed by these voice samples and feed them to a not so highly dense convolutional network with proper regularization parameters to remove the over fitting of data. As for the Biospecimen and the Biomarkers in Cerebrospinal Fluid features part we got a refined dataset from PPMI which will be good to go once some null values and outliers will be removed in the preprocessing.

SIGNIFICANCE, ORIGINALITY AND CREATIVITY OF WORK

As mentioned above Deep Learning is one of the finest developments recently gaining a lot of popularity in state of the art medical researches across the globe. But, There have been a very few research works on Parkinson Detection based on Deep Learning. We in our study understand the importance and need for Deep Learning techniques in image or voice based classifications, segmentations, and studies where we have to work around non-linear features which result in non-linear decision boundary. And we suggest for better and efficient results Deep Learning techniques should be used widely to detect Parkinson Disease. We want to create a model different from the previous work done and aim for better accuracy and less work load on the hardware. We wanted to take a step ahead and increase the count of quality studies on PD detection based on Deep Learning and hence we chose this project. Moreover, the novelty of this study is not just the Deep Learning models we are planning to implement but also the various feature-set mentioned above. We want to contribute and innovate a model whose prediction accuracy could reduce the numbers of deaths and millions of dollars spent on the treatment of this disease throughout the world by using minimum resources and provide a cheap alternate.

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