

A Novel Scheme for detection of Parkinson's disorder from Hand-eye Co-ordination behavior and DaTscan Images

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Abstract

With millions of people across the globe suffering from Parkinson's disease (PD), an objective, confirmatory test for the same is yet to be developed. This research aims to develop a system which can assist the doctor in objectively saying whether the patient is normal or under risk of PD. The proposed work combines the eye-hand co-ordination behaviour with the DaTscan images in order to determine the risk of this disorder. Initially, eye-hand coordination level of the patient is assessed through a hardware module. Then, the DaTscan image is analysed and used to extract certain geometrical parameters which shall indicate the presence of PD. These parameters are then finally fed into a Multi-Layer Perceptron Neural Network using Levenberg-Marquardt (LM) Back propagation training algorithm. Experimental results indicate that the proposed system exhibits an accuracy of around 93%.

Keywords: Parkinson's Disease(PD), Eye-hand Co-ordination, DaTscan images, Multi-Layer Perceptron(MLP), Back Propagation (BP).

1. Introduction

Recent statistics provided by WHO indicates that approximately 1 billion people are suffering from various neurological diseases like Wilson's disease, Parkinson's disease (PD), Tics, or Dystonia, worldwide. The count of the people affected by PD is around 7 to 10 million on a global scale [1]. PD is more common in the elderly, with most cases occurring after the age of 50 [2]. Right now, there are no concrete testing procedures for the diagnosis of PD, and the clinical diagnosis is taking into account the presence of cardinal indications and the reaction of the subject to PD medications (primarily levodopa) [3-4]. Unified Parkinson's disease Rating Scale (UPDRS) is utilized to gauge the severity of PD [5].

The accuracy of medical diagnosis for these neurological disorders depends largely on the interpretation of medical images [6]. This approach is not extremely precise as at least 15% of patients with a diagnosis of Parkinson's disease in the population do not fulfill strict clinical criteria for the disorder, and roughly 20% of patients with Parkinson's disorder who have as of now come to therapeutic consideration have not been diagnosed as such [7]. It is very important to diagnose PD accurately since if the patient is misdiagnosed as healthy, his condition will worsens over time [8].

All of the above mentioned neuro-disorders, including PD, have movement related manifestations, which are difficult to contain. The disease affects a part of the brain known as the "substantia nigra", which controls movement in the body [9]. This region has neurons which produce a chemical known as "Dopamine". Among the Parkinson's patients, 80 % or a greater amount of these dopamine-creating cells are harmed, dead, or generally deteriorated. Eventually the neurons are forced to fire wildly, leaving patients not able to control their movements [10]. There are four cardinal features of PD that can be grouped under the acronym TRAP: Tremor at rest, Rigidity, Akinesia (or bradykinesia) and Postural instability [11]. These physical manifestations deteriorate the quality of the life the person is leading in many ways. If these physiological symptoms are monitored at an early stage, necessary precautions and medications can be taken to control the severity of the disorder, thus increasing the quality of life lead by the patient. The focus of this work is to develop a system, which can assist doctors and bio-informatics practitioners in the diagnosis of PD in the early stages itself by monitoring the changes in the putamen and caudate regions of the brain and by measuring the eye-hand coordination level. This will aid in ruling out parkinsonism (essential tremor or drug-induced parkinsonism).

Bradykinesia is clinically assessed using rapidly alternating movements, such as finger-tapping, where the patient is asked to repeatedly tap together their thumb and forefinger [12]. Bradykinesia is being assessed through eye-hand coordination level. Currently, to measure eye-hand coordination level, sophisticated equipment use high-end accelerometers, electromyography and computer tracking. Each of these solutions has exhibited restricted convenience in clinical settings because of their deficiencies in wearability, fidelity, and flexibility [13]. A drawback of the accelerometers is that the amplitude of the measured accelerations of a moving segment depends on the position of the sensor on the segment [14].

Investigating the striatal dopamine transporter status by means of brain imaging techniques have been recommended to enhance the diagnostic accuracy in the case of Parkinson Disease [15 & 41]. Various brain imaging techniques like DaTscan, Transcranial Sonography, MRI and PET scans could be analysed. Yet, not all these scans are viable

options for implementation. Transcranial Sonography scan has been reported to have sensitivities as low as 50% for clinically probable PD [16]. Anatomical imaging modalities like MRI were not well suited to describe the behavior of PD. Recent clinical studies indicate that the DaTscan images could describe the behavior of PD by mapping the level of dopamine secretion.

Several research works were carried out using DaTscan images to identify the presence of PD [17-19]. These methods utilize either textural features or statistical features to describe the risk of this disorder. Once the significant features are extracted, the next phase is to develop an efficient classifier. Researches over the past three decades indicate that neural networks are employed as a strong tool for developing various kinds of classification and prediction system. These algorithms are applied for various systems like medical diagnostic systems [20], disease prediction systems [21-22], several variants of expert systems etc. But the accuracy of these methods solely depends on the kind of features extracted pertaining to each disorder.

This research introduces a basic system which combines the eye-hand co-ordination behaviour with the features extracted from the DaTscan images in order to determine the risk of Parkinson's disorder.

2. Proposed System

The proposed system consists of 2 different processing modules namely eye-hand coordination system and the image processing module. A broad outline about the proposed system is presented in Fig. 1.

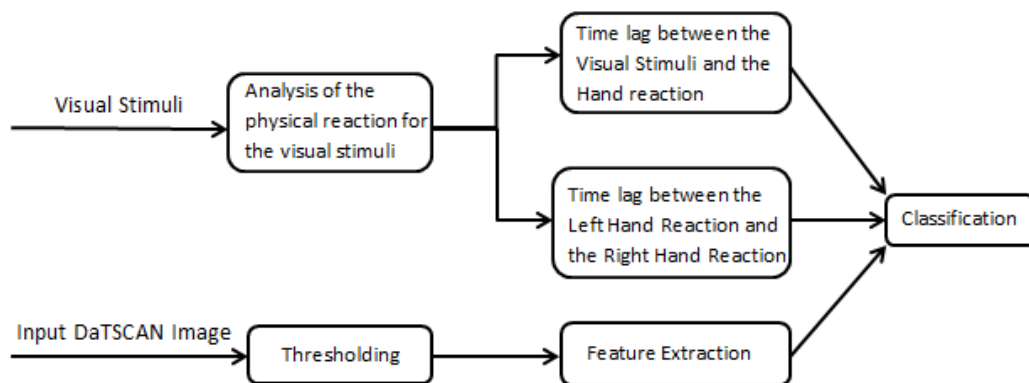


Fig. 1. General Workflow of the Proposed System.

2.1 Determination of Eye-Hand Coordination

One of the primary symptoms of PD is the loss of motor control of a patient. Given the basic significance of hand-eye coordination among all the psycho-motor skills, it is important to diagnose related developmental delays and its issues within the near future [23]. The correct classification of movement patterns, slight and deviating from normal, is the challenge of diagnosis of PD [24]. Proficient and precise evaluation of tremor and

bradykinesia (slow motor movement) utilizing objective techniques might, in any case, improve diagnostic specificity and provide un-biased quantification of therapeutic interventions [25]. Also, it has been inferred that increased reaction time (~350 ms) for PD affected patients as compared to normal people (~250 ms) leads to tremors in the patient [26]. Thus, to ascertain whether there is a need of looking into the possibility of the onset of PD, a preliminary test to diagnose hand-eye coordination issues is required.

2.1.1. Electronic Circuitry Module

The input to this system is a visual stimulus, which is the blinking of a LED at random intervals of time. On seeing the flash of the LED, the patient should press 2 switches, one in each of his hands. The circuitry setup for this module is presented in Fig. 2. Two features are calculated from the above setup. First is the time lag between flashing of the LED and reception of the first signal from either of the switches. Second is the time difference between the reception of the signal from left and right switches. These measured time parameters are given as feature inputs to a neural network at a later stage.

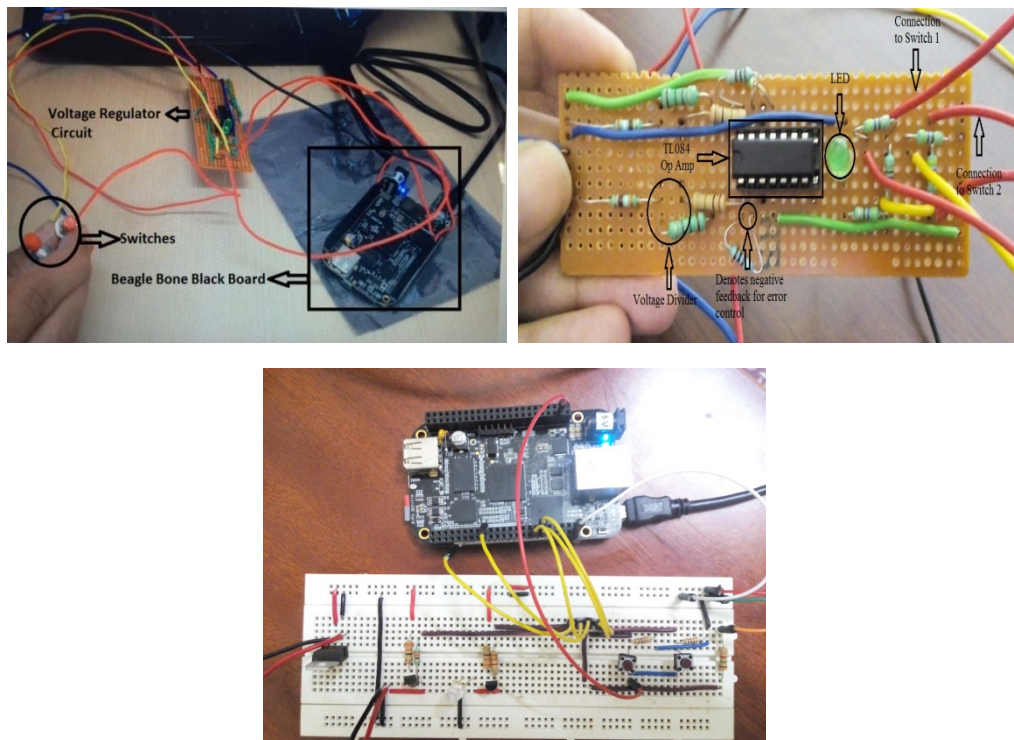


Fig. 2. Eye-Hand Coordination Test Module with Switches and Beagle Bone Board.

The observations for the time lag between flashing of the LED and reception of the first signal in the eye-hand co-ordination module was presented in Table 1. Also, from Fig. 3 and 4, a clear demarcation can be observed between the time lag seen for normal and abnormal patients. The parameter 'Time lag parameter_1' measures the lag between flashing of the LED and reception of the first signal from either of the switches. For normal

volunteers, the time lag ranges from 251-261 milliseconds, whereas for abnormal patients it ranges from 346-370 milliseconds. The parameter ‘Time lag parameter_2’ time difference between the reception of the signal from left and right switches. For normal controls, this parameter varies from 21-29 milliseconds, whereas for abnormal patients it ranges from 51-65 milliseconds. Hence, if the reading of the time lag for a person is above 346 ms and 50 ms for the measured parameters, it can be inferred that a person may be susceptible to Parkinson’s Disease and hence needs to undergo further diagnosis.

Table 1. Time lag parameters for normal and abnormal controls.

S.No	Type of control	Time lag parameter_1 in milliseconds	Time lag parameter_2 in milliseconds
1	Normal_Patient_1	251	23
2	Normal_Patient_2	255	27
3	Normal_Patient_3	250	21
4	Normal_Patient_4	257	23
5	Normal_Patient_5	250	22
6	Normal_Patient_6	259	27
7	Normal_Patient_7	261	29
8	Abnormal_Patient_1	352	62
9	Abnormal_Patient_2	346	57
10	Abnormal_Patient_3	365	55
11	Abnormal_Patient_4	361	51
12	Abnormal_Patient_5	359	65
13	Abnormal_Patient_6	370	65
14	Abnormal_Patient_7	369	63
15	Abnormal_Patient_8	350	62

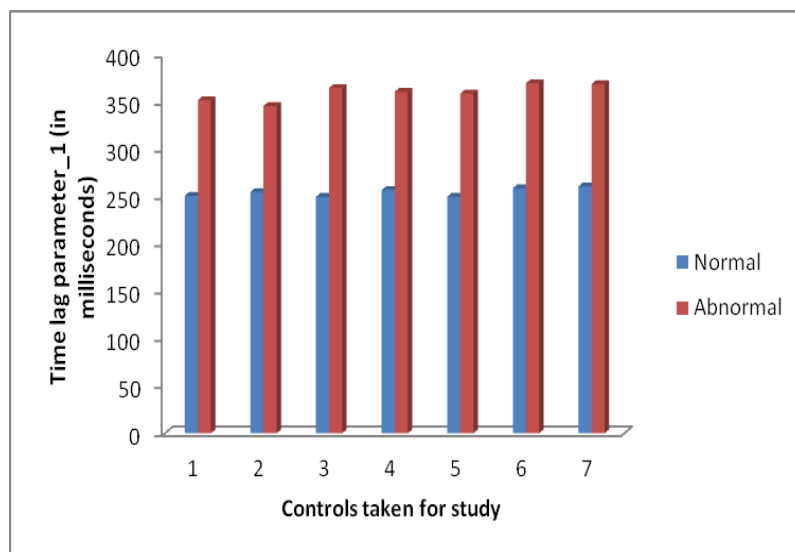


Fig. 3. Time Lag for first signal reception for normal and abnormal patients.

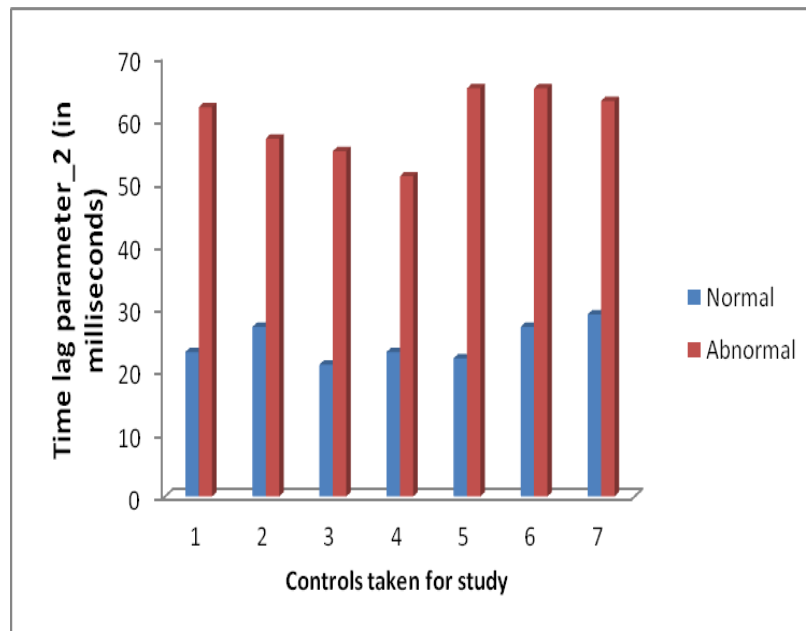


Fig. 4. Time Lag for second signal reception for normal and abnormal patients.

2.2 Image Processing Module

The DaTScan images are obtained from the PPMI database for initial analysis [27]. For identification of PD and other related diseases, the Putamen and caudate area of the DaTscan needs to be analyzed and the sample images are presented in Fig. 5. It has been seen that the uptake of dopamine in the Putamen region in a PD affected patient is much lower as compared to dopamine uptake level in a normal person. In a few experiments done already by others, patients with advanced bilateral PD have basically no uptake in the putamen, with altogether diminished uptake in the caudate nucleus [28].

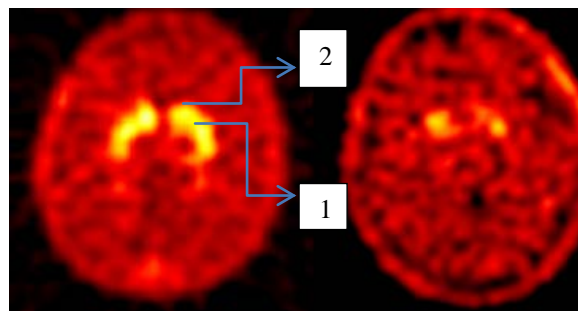


Fig. 5. 1: Caudate 2: Putamen. Left image is the DaTscan of a healthy person and right image is the DaTscan of PD affected patient.

A dynamic methodology which is independent of the demographic components: age - atrophy variance, sex-volumetric changes, and races-shape of the brain is required [29]. The shape of the putamen-caudate region changes from a comma-shape to a much smaller circular-shape. Hence, the ROI would be the Putamen and Caudate, from which we shall be extracting several features for our analysis.

Edge detection and image analysis are two very important steps in many of these image processing applications [30]. Manual Region of Interest (ROI) analysis is dependent on the subjective drawing of the ROI, which may give rise to bias [31]. Hence, ROI is selected by using the edge detection technique, where threshold is used as a selection parameter.

2.2.1 Thresholding

It has been observed that the ROI appears as a white bright spot as compared to the grey background in a DaTscan image. Hence, for extracting the ROI, intensity based selection process is most appropriate. One of the Primary advantages of employing thresholding techniques is that they are computationally inexpensive and hence do not demand a large apportionment of computational time and power [32].

In thresholding technique, edges that arise from abrupt changes in the intensity profile of the image are called as Intensity edges [33-35]. These intensities of gray level changes are plotted as a histogram distribution. In the histograms presented in Fig. 6, it can be seen that the bins of the intensity range 252-255 have maximum count and correspond to the caudate and putamen region. Therefore, this range is set as the threshold. Using this threshold, the ROI is selected in the images. After which, a binary mask is to highlight only the ROI is made. Here, the ROI is given the value of logic '1', and the rest of the image give intensity value as logic '0'. A sample input image and its thresholded results are presented in Fig. 7 and 8.

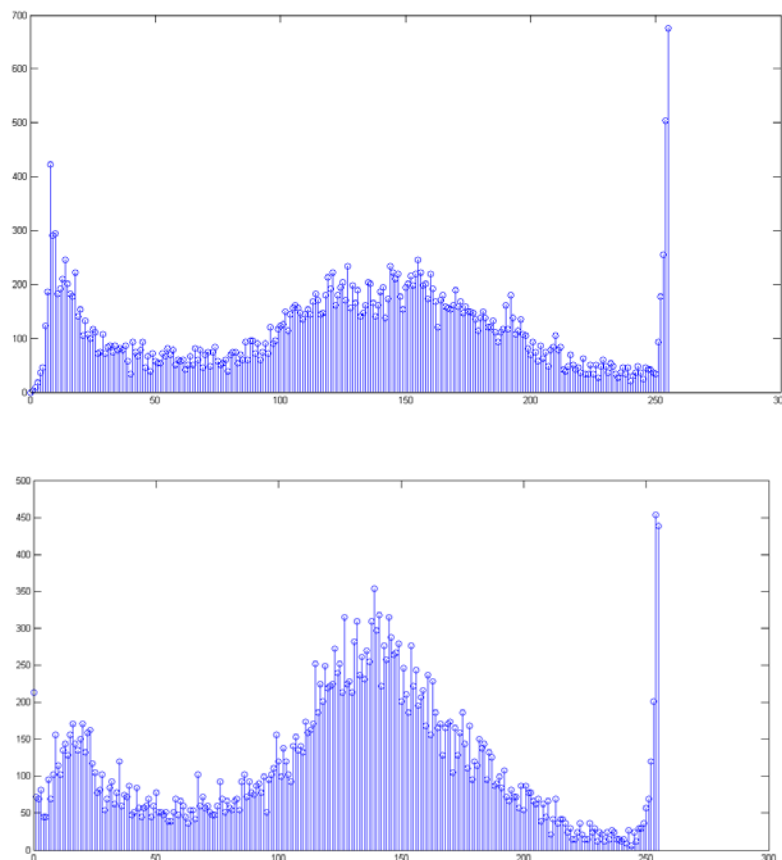


Fig. 6. Histogram Distribution of the DaTSCAN images.

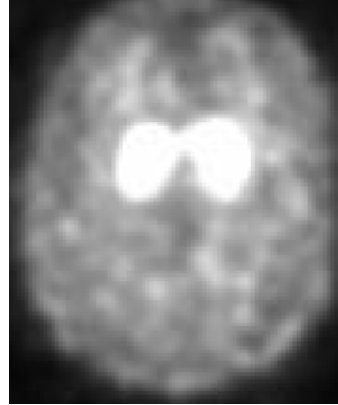


Fig. 7. The input DaTscan image

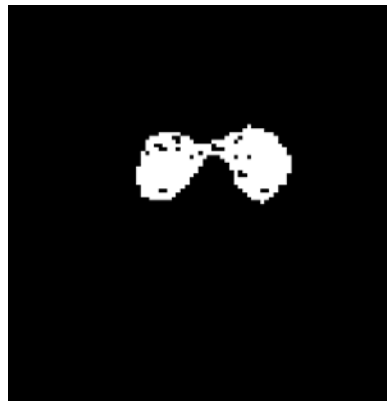


Fig. 8. The ROI extracted from the input image.

2.2.2 Feature Extraction

Three geometrical features need to be extracted from the DaTscan images. These intrinsic features of images could be utilized to classify them into distinct classes [36]. Geometrical parameters like area, distance and ratio intensity of ROI and the background area have been chosen as these can be accurately calculated from the ROI without any ambiguity. Also, since the geometric shape of the Putamen and Caudate region changes as the severity of the disease progresses, it is important to take into consideration these geometric parameters

It has been observed that area of the ROI decreases as the 2 putamen and caudate region merge into one as severity increases. The distance between the left most and right most point also varies significantly. The following are the features which need to be extracted from the input images:

- a) The ratio of intensity of ROI and the Background area:
The intensity normalization consists of comparing the uptake value in areas of specific activity (binding to dopaminergic transporters) to the value in areas of non-specific activity (vascular activity) between subjects [37]. The ratio of intensity has been calculated, by taking the ratio of pixel values of the putamen region and the pixels in the background region.
- b) The area of the ROI (putamen and caudate) :
This area represents the number of pixels within the boundary is calculated. This is done by summing the number of '1' present within the ROI which is indicative of the area of Putamen. It is calculated according to the following equation 1.

$$A = \sum f(x, y) \quad (1)$$

In the above relation, A denotes the area being calculated, f(x,y) denotes the pixel value at the coordinates (x,y).

- c) The distance between the left most and right most point of the ROI :
To extract the location feature, Euclidean distance is measured [38]. The image is first scanned from the right side to the left, and then from the left side to the right side for an intensity value of '1'. By, doing this, we shall know the index rightmost and leftmost point of the ROI. Now, the distance between these points is calculated, using the relation presented in equation 2. The resultant inference obtained is presented in **Table 2**.

$$D = \sqrt{(y1 - y2)^2 + (x1 - x2)^2} \quad (2)$$

where 'D' is the distance being calculated, (x1,y1) are the coordinates of the leftmost point and (x2,y2) are the coordinates of the rightmost point.

Table 2. Extracted feature values

Type of the Image	Area of ROI (pixels)	Max Distance	Ratio of Intensity
Normal_Patient_1	404	34.7131	1.5975
Normal_Patient_2	451	36.4966	2.4423
Normal_Patient_3	410	41.0000	1.6776
Normal_Patient_4	428	37.1079	1.7162
Normal_Patient_5	564	36.2215	2.0819
Normal_Patient_6	414	34.7131	1.8345
Normal_Patient_7	537	39.0128	1.9843
Abnormal_Patient_1	275	53.5350	1.3316
Abnormal_Patient_2	287	43.5737	1.0121
Abnormal_Patient_3	370	41.7732	1.5562
Abnormal_Patient_4	303	50.6063	1.1351
Abnormal_Patient_5	321	50.0399	1.3655
Abnormal_Patient_6	368	53.9351	1.5582
Abnormal_Patient_7	370	53.5350	1.5776
Abnormal_Patient_8	391	56.4358	1.5849

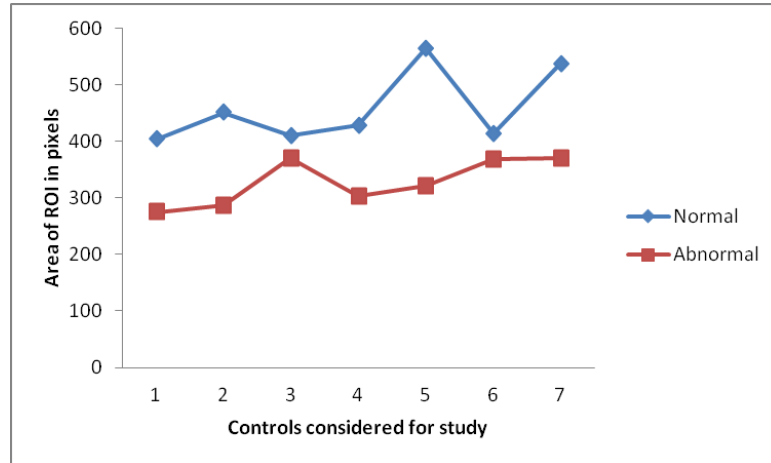


Fig. 9. Comparison of Area of ROI for Normal and Abnormal Patients.

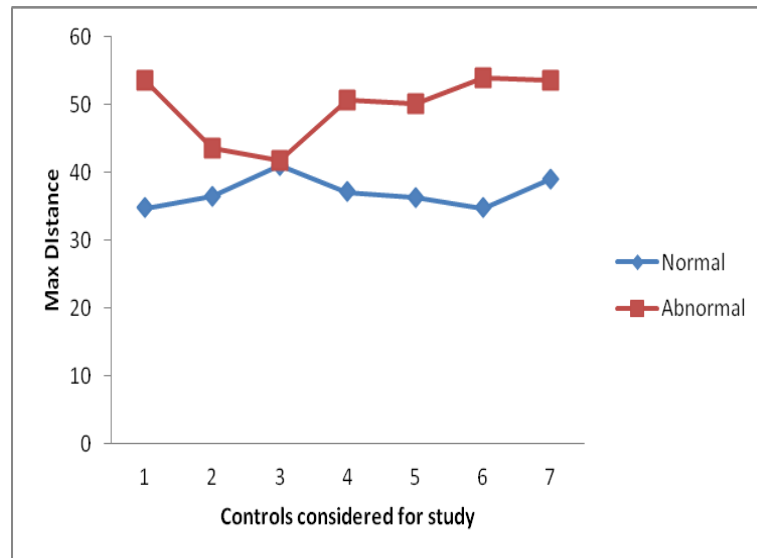


Fig. 10 Comparison of Max. Distance for Normal and Abnormal Patients.

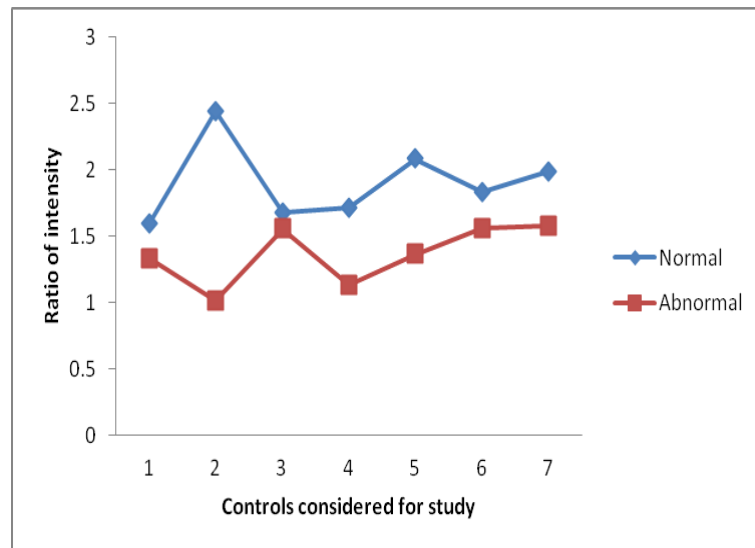


Fig. 11. Comparison of Ratio of Intensity for Normal And Abnormal Patients.

2.3 Classification

Once the significant features are extracted, they should be trained using a suitable algorithm to develop a classification model. In this research, Multi-Layer Perceptron based neural network is employed for classification. The extracted features from both the modules are fed to a feed forward neural network for classification. This module will give the final output which will determine whether the person is normal or has some abnormality.

2.3.1 Architecture

Here, since there are 5 features to be given as inputs, there are 5 neurons in the input layer. There are 2 hidden layers with 9 and 8 neurons respectively. After which there is one final output neuron. This architecture was finalized after observing the accuracy rate between different setups. The neural network architecture is presented in Fig. 12

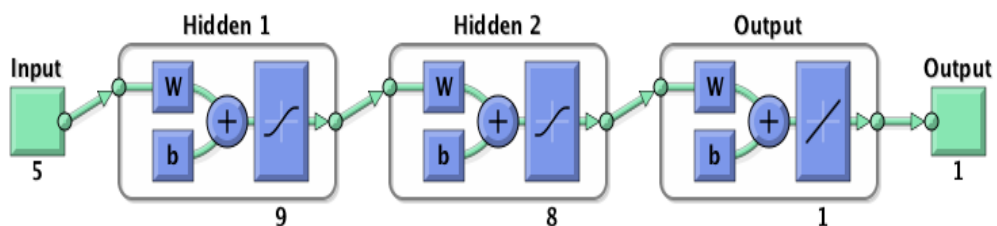


Fig. 12. Architecture of the neural network used.

For comparison of accuracy of the proposed system against the accuracy of the system without the hardware module, we create another neural network. This neural network architecture is similar to the previous architecture to maintain fairness in comparison. But the only change being the number of input neurons is just 3. These 3 input neurons correspond to the three features extracted from the DaTSCAN image. The architecture for this is given below in Fig. 13.

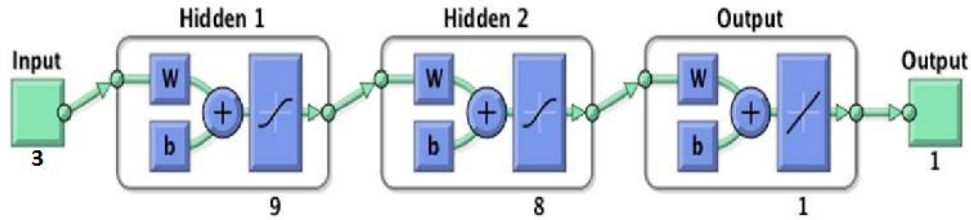


Fig. 13. Architecture of the neural network without input from the hardware module.

2.3.2 Training

The following criteria must be studied when benchmarking neural network algorithms:

- Training time
- Number of iterations required
- Convergence of algorithm

After taking the above criteria into consideration, Back Propagation (BP) algorithm was chosen as the most appropriate solution [39]. In BP, Error data at the output layer is back propagated to earlier ones, allowing incoming weights to these layers to be updated [40]. Many variations of the back propagation algorithm exist, which vary according to the training algorithms namely Levenberg-Marquardt (LM), Conjugate Gradient (SCG), Resilient Back propagation (RP) and One-Step Secant back propagation (OSS).

The features extracted were trained using these algorithms and the resultant observations are presented in **Table 3**.

Table 3. Performance of various training algorithms.

Algorithm	No. of Epochs	Time (hr:min:sec)	MSE at Epoch
LM	5000	0:04:22	2.6363e-20
RP	235	0:00:12	2.0073e-05
OSS	144	0:00:03	1.5868e-05
SCG	215	0:00:22	8.5384e-07

From the above observation, it can be inferred that Mean Squared Error (MSE) is least for LM algorithm, as compared to the other algorithms. The performance plots of each of these algorithms are presented in **Fig. 14-17**.

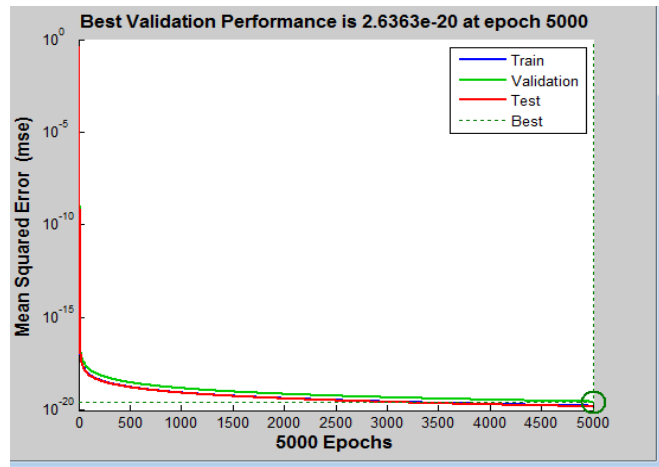


Fig. 14. MSE for LM algorithm.

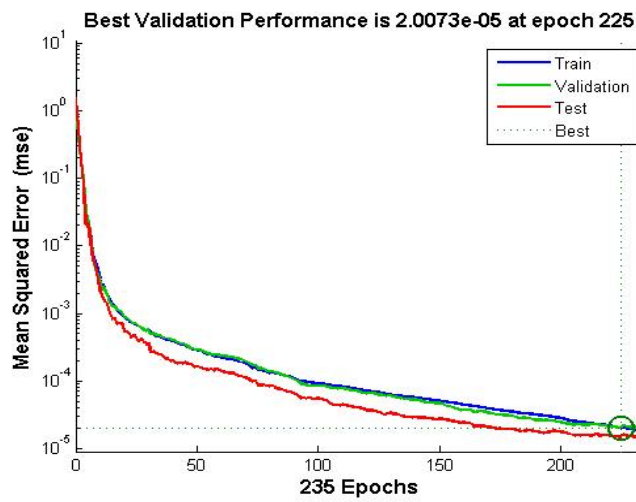


Fig. 15. MSE for RP algorithm.

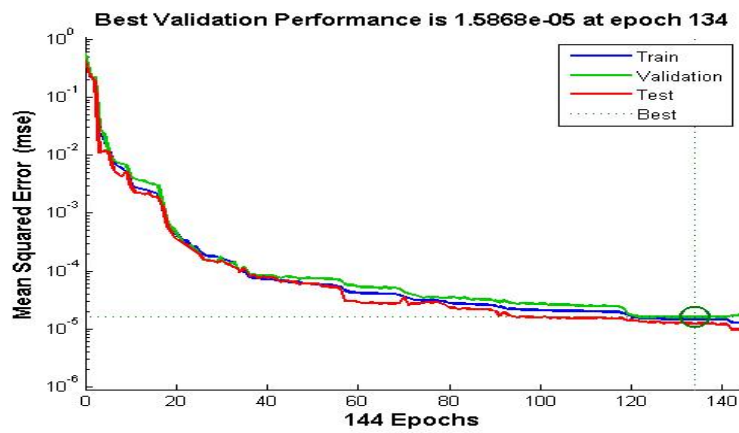


Fig. 16. MSE for OSS algorithm.

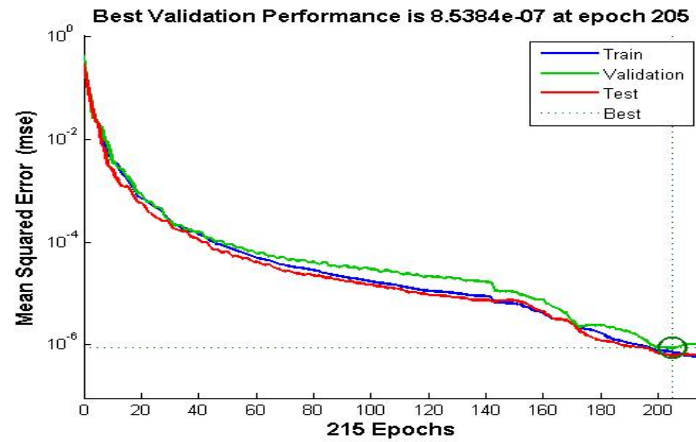


Fig. 17. MSE for SCG algorithm.

From the above figures, it can be seen that speed of convergence is highest for LM algorithm as it attains a saturation value the fastest. Hence, the algorithm used for classification is LM.

3. RESULTS AND DISCUSSIONS

The following observations were made from the numerical values of the extracted features

- As the severity of the PD increases, the area of Putamen and Caudate region decreases. From Fig. 9, it can be seen that the range of values for ROI area for normal patients was between 404 and 537, whereas for the PD affected patients it was observed to be between 275 and 391.
- The distance between the leftmost point of Putamen-Caudate region to the rightmost point seemed to increase as the severity of PD increased. As observed from Fig. 10, The normal values lay between 32 and 39, whereas abnormal values were between 41 and 53.
- The ratio of intensity of ROI and background varied very minimally as can be inferred from Fig.11. For the normal set, the values were lower and varied from 1.01 to 1.55. For the abnormal set, these values varied from 1.72 to 2.44.

Thus a clear demarcation could be seen between the values observed for the normal and abnormal set. Therefore, these values are given to a MLP neural network for training and testing. LM algorithm is used for classification and the corresponding error histogram for the same is presented in **Fig. 18**.

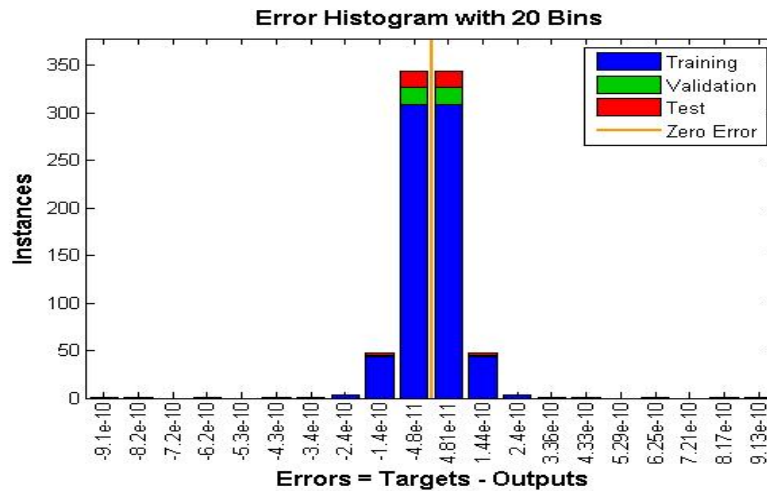


Fig. 18. Error Histogram of LM trained MLP neural network.

The ratio of division of the data set for training and testing is 0.8:0.2. Now, using this neural network, the features extracted from a new DaTscan image needs to be classified as ‘Normal’ or ‘Abnormal’. The accuracy of such classification with LM Back propagation training algorithm is found out to be approximately 93.0%. Also, in order to prove the effectiveness of combining eye-hand co-ordination module with DaTscan image processing, the proposed work was carried out without including eye-hand co-ordination module. Interestingly, the accuracy obtained was approximately 87%.

4. Conclusion

The aim of this research work was to develop a basic system which can objectively diagnose Parkinson’s disease through certain symptoms as well as with the DaTscan image of the patient. This has been achieved with an accuracy of 93% by firstly measuring the eye –hand coordination level of the patient and then by processing the scan image for extracting certain features which aid in diagnosis of PD. Such a system will be highly helpful to doctors for confirming the presence of this neuro-disorder, thereby decreasing the occurrence of misdiagnosis. Future work will include quantifying symptoms like Resting tremor and rigidity and including these as features for classification.

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