Early Prediction of Parkinson’s Disease using Artificial Neural Network

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Abstract

Objectives: The objective of this work is to present an in-depth understanding of the diagnosis of Parkinson's Disease (PD) is critical for efficacious neuroprotection in the early stage. Diagnostic tools based on machine learning techniques using Striatal Binding Ratio (SBR) of Caudate and Putamen (left and right) are very useful to identify early PD. Methods: This paper presents an approach to develop an ANN model for prediction of Gamma-Amino Butyric Acid (GABA) concentration level for PD and Healthy Group (HG). Using multilayer perception network having 4-30-1 architecture for predicting GABA concentration level. The network is trained to an optimum level and trained network that predicts the GABA concentration level for the interpolated values of input parameters like Striatal Binding Ratio (SBR) of Caudate left, Caudate right and Putamen left, Putamen right. Findings: According to the ANN model, the prediction performance is highly encouraging with minimum error and high accuracy. The intended prediction model for GABA concentration level overcomes misdiagnosis of early PD. Applications: We propose to study the improvement of the early prediction of Parkinson's disease, by implementing the ANN. The predictive model for diagnosing Parkinson disease using artificial neural network is efficient in early detection of neurogenerative disorders.

Keywords: Artificial Neural Network, Early Prediction, GABA, Parkinson's Disease, Striatal Binding Ratio

1. Introduction

Parkinson's Disease is a chronic gradual neurodegenerative disorder which evidently affects the neural cells of the human brain called the substantia nigra. These neurons generate dopamine content, an inhibitory neurotransmitter that transmits signals which coordinate smooth movement. The PD is due to the death of dopamine transporters and as a result gait system is affected. The clinical motor symptoms are impairment of movement with tremor, Gait problem, slowness, stiffness, or balance problems and impairment of posture. The calculation of dopamine deficiency in the caudate and putamen of SPECT images of the human mid brain is the significant diagnostic tool for discriminating PD patients from the healthy group.

Gamma-Amino Butyric Acid (GABA) is a most essential neurotransmitter widely distributed throughout the Central Nervous System (CNS). GABA mediates presynaptic inhibition of primary blood vessels in the motor neuron system. It regulates brain excitability. Too much excitement can lead to irritability, restlessness, insomnia, seizures, and movement disorders; it must be balanced with inhibition. Low GABA level causes neurological disorders including Parkinson's disease, anxiety, depression, insomnia, and epilepsy. The radio receptor assay technique is used to measure GABA concentration level for detecting PD.

Recently the Artificial Neural Network acts as a prediction and modeling tool for diagnosing various diseases in different medical areas. ANN has weighted-interconnected nodes called stimulated neurons and has the ability of the human brain. It can learn from the past experiences and find solutions for complex nonlinear multidimensional functional relationships. The unique characteristic is describing the relationship between training and testing datasets from a large number of inputs without any prescribed structure about the problem. The
three layered feed-forward with Levenberg-Marquardt (LM) training algorithm serves as an effective, simple, better, fast, compact and efficient tool for predicting mechanical properties\textsuperscript{12-14}.

Diagnostic tool used in machine learning techniques such as Support Vector Machine (SVM), Multivariate Logistic Regression (MLR) and Artificial Neural Network (ANN) is used to construct a prediction model for diagnosing neural disorders\textsuperscript{15}. Since, they allow individual level characterization, high level of clinical translation is potentially obtained. They use multivariate and supervised learning techniques with complex high dimensional feature space to train the network. The input datasets are categorized based on the trained network. SVM finds hyper plane to classify the subjects into early PD and healthy group. MLR determines the probability based on SBR values to discriminate early PD subjects from healthy group. ANN uses input data to train the neural network and the trained network classifies datasets\textsuperscript{16,17}.

In the related work, features are extracted from the striatum and the effective feature reduction techniques like Principal Component Analysis (PCA), Independent Component Analysis (ICA) are used to pick up the required features. This makes the system very complex\textsuperscript{18}.

In this present work, only four features of Striatal Binding Ratio (SBR) values, namely Caudate left, Caudate right and Putamen left, Putamen right are obtained from Parkinson’s Progress Markers Initiative (PPMI) database which focuses on identifying PD progressive biomarkers that determine PD\textsuperscript{19}. We also investigate the level of GABA concentration of Parkinson disease and healthy group using SBR values. The Predictive models using ANN architecture are developed to GABA concentration level based on SBR (Caudate left, right and Putamen left, right) values.

### 2. Computational Methods

#### 2.1 PPMI Database

The input features are obtained from the international PPMI database. All PD subjects are in an early stage of the disease within two years\textsuperscript{20}. The corresponding SBR values are taken for the analysis.

#### 2.2 Calculation of SBR Values

Iterative reconstruction is performed on SPECT raw projection data using Hybrid Ordered Subset Expectation Maximization (HOSEM) algorithm. Iterative reconstruction is done without any filtering to ensure consistency of the reconstructions. The reconstructed HOSEM files are processed for Attenuation correction, which is filtered and normalized to get the same anatomical alignment. Striatal uptake count densities of the Region Of Interest (ROI) are extracted and used to evaluate Striatal Binding Ratios (SBRs) for each region of the four striatal regions. SBR is calculated by PPMI as follows and compared with Occipital cortex region below the Putamen as reference region\textsuperscript{21}.

\[
SBR = \frac{\text{target region}}{\text{reference region}} - 1 \quad (1)
\]

Where,

- Target region is referred as left caudate, right caudate, left putamen, right putamen
- Reference region is referred as occipital cortex

Table 1 shows the number of observations and averaged SBR values.

#### 2.3 Artificial Neural Networks

The ANN is inspired by the biological nervous system and is used to solve a wide range variety of complex scientific problems\textsuperscript{22}. Neural networks are suited for biological counterparts, they can learn, and therefore can be trained to find solutions, recognize patterns, classify data, and forecast future events. A neural network is a system composed of many simple processing elements operating in parallel, whose function is determined by the network structure, connection strengths, and the processing performed at computing elements or nodes\textsuperscript{23}. ANN resembles the human brain in two respects: 1. Knowledge is obtained from the network by learning process and 2. Interneuron connection strengths (synaptic weights) are effectively adjusted to store the knowledge\textsuperscript{24}. The fundamental unit of the ANN is defined as artificial neuron (or neuron). The neuron has a set of inputs ($X_i$) weighted...
before reaching the main body of the processing element by the connection strength or the weight \( w \) (i.e., \( X_i \) is multiplied by \( w_j \)). In addition, it has a bias term, a threshold value that has to be reached or exceeded for the neuron to produce a signal, a non-linearity function \( f_i \) that acts on the produced signal \( R_i \), and an output \( O_i \). The basic model of a neuron is illustrated in Figure 1.

**Figure 1. Basic neuron model.**

### 2.4 ANN Architecture

In Artificial neural network architecture commonly consists of Input layer, Output layer and the Hidden layers as shown in Figure 2. Add more number of hidden layers where the size of the input is large to extract higher-order statistics.

**Figure 2. ANN architecture.**

The input signal propagates through the network in a forward direction, on a layer-by-layer basis. These networks are commonly referred to as Multilayer Perceptrons (MLP). The hidden layers help to add non-linearity to the system and address interactions between input variables. Choosing the number of hidden layers is the important factor to be considered while solving a ANN problem.

### 2.5 Implementation

In the present work, an ANN was modeled using a Network Fitting (NF) tool box of MATLabV2013. NF tool is an acronym for network fitting tool with Graphic User Interface (GUI) module. The data were further divided into training sets, validation set and testing set in the proportions of 70:15:15 respectively. The network was trained by using Levenberg-Marquardt Back Propagation (LMBP) algorithm, with Mean Square Error (MSE) as the performance measuring the parameter.

The back propagation neural network was designed based on delta rule, called steepest descent algorithm. It consists of a forward pass of input, hidden and output training samples. A backward pass of the sample is made to update the weight \( \omega_{ij} \) of all neurons \( i \) in layer \( k \). One epoch is presented to the network when a forward pass and backward pass have made. The forward pass output will be

\[
\zeta_k(n) = \sum_{j=0}^{m} \omega_{kj}(n) \gamma_j(n)
\]

Where
- \( n \) – No of conducted epochs
- \( k \) – No of layers
- \( \omega \) – Current weight vector
- \( m \) – No of neurons in layer \( k \)

\( \gamma \) is the output vector from the previous defined as

\[
\gamma_i(U_j)(n) = \alpha_{ij}(\zeta_j(n))
\]

The error in the forward pass output layer is represented as the difference between the predicted value and the desired value \( d \) as the overall squared error.

\[
\epsilon_k(n) = \frac{1}{2} \sum_{j=0}^{m} \left[ d_j(n) - \gamma_j(n) \right]^2
\]

Differentiating \( \epsilon \) with respect to \( \zeta_j \), the delta rule is obtained as

\[
\Delta \omega_{kj}(n) = - \eta \frac{\partial \epsilon}{\partial \omega_{kj}(n)}
\]

Where \( \eta \) is defined as learning rate

The LM training algorithm is used in this study by modifying the steepest descendent rule. The LM training algorithm can be obtained.
LM is the faster, more accurate with minimum error algorithm. Compared to the steepest descendant rule. The error function is given with a Taylor expansion

\[ e(n + \delta) = e(n) + J(n) \delta \]  

(6)

Where \( J(n) \) is the Jacobian matrix^3.

In this study, the input layer with four neurons representing the four variables viz. Caudate (L), Caudate (R), Putamen (L) and Putamen (R) were used and the hidden layer consisted of 30 neurons with log-sig activation function. The output layer with one neuron was used to model the network. This model was used to predict GABA concentration level for PD and Healthy Group (HG). The MSE of early PD and healthy group is shown in Table 2.

| Table 2. MSE for Early PD and Healthy group |
|----------------------------------------|
|                                       |
| GABA Error                | Measured | Predicted | Error   |
| Early PD               | 0.155    | 0.154817  | 0.000   |
| Healthy group       | 0.782122699 | 0.783354299 | 0.00123 |

3. Results and Discussions

3.1 Effect of SBR Values on GABA Concentration Level for PD

Based on the SBR values of Caudate (L), Caudate (R), Putamen (L) and Putamen (R) the predictive model of GABA concentration level for PD is developed by ANN. Regression plot and performance plot are drawn to study the error and accuracy. Figure 3 shows the regression plot for PD. The plot shows the average regression value (R=0.99954) is almost 1. It indicates that the predicted values and the output values are lie on the fit. Similarly, the same study is implemented for training, testing and validation.

Figure 4 shows the performance of the network is measured using Mean Square Error (MSE) over the epochs. It means that the network is carried out number of iterations in order to attain good accuracy with minimum error. The ANN attained a stable state after 12 cycles of training. Figure 4 shows the error curve of training. From the Graph it is clear that the error is minimized by iterations carried out by the network during training, validation and testing. Generalization is stopped at the 18th epoch. The best performance is obtained at the 12th epoch. The MSE during training and validation was found to be 1.7677e-07.

Figure 4. The MSE performance plot of ANN for PD.

Figure 3. The regression plots of training, testing, validation and average of all sets for PD.

Figure 5. Comparison of GABA concentration level of PD among measured and predicted values.
The measured values and predicted values of GABA concentration level are plotted as shown in Figure 5. From the comparison, it clearly shows that the models predict the GABA concentration level with reasonable accuracy.

3.2 Effect of SBR Values on GABA Concentration Level for HG

Similarly, based on the SBR values of Caudate (L), Caudate (R), Putamen (L) and Putamen (R) the predictive model of GABA concentration level for HG is developed by ANN. Regression plot and performance plot are drawn to study the error and accuracy. Figure 6 shows the regression plot for HG. The plot shows the average regression value (R=0.9981) is almost 1. It indicates that the predicted values and the output are lie on the fit. Similarly, the same study is implemented for training, testing and validation.

Figure 6. The regression plots of training, testing, validation and average of all sets for HG.

Figure 7 shows the performance of the network is measured using MSE over the epochs. It means that the network is carried out number of iterations in order to attain good accuracy with minimum error. The ANN attained a stable state after 11 cycles of training. Figure 7 shows the error curve of training. From the Graph it is clear that the error is minimized by iterations carried out by the network during training, validation and testing. Generalization was stopped at the 17th epoch. The best performance is obtained at the 11th epoch. The MSE during training and validation was found to be 0.0025906.

The measured values and predicted values of GABA concentration level were plotted as shown in Figure 8. From the comparison, it clearly shows that the models predict the GABA concentration level with reasonable accuracy.

Figure 7. The MSE performance plot of ANN for HG.

Figure 8. Comparison of GABA concentration level of HG among measured and predicted values.

4. Conclusion

The significant conclusions have been drawn from the proposed prediction system: Striatal Binding Ratio (SBR) values for the four striatal regions (left and right caudate, and left and right putamen) obtained from the Parkinson’s Progression Marker’s Initiative (PPMI) database. A multilayer ANN network having neurons of 4-30-1 architecture is found. The network is trained the SBR values and the trained network generates the predictive models for GABA concentration level based on SBR (left, right...
Caudate, left, right Putamen) values of PD patients and healthy group. These models have the potential to distinguish Early PD from healthy group. The regression plots for PD and healthy group are obtained. The average regression value shows a close correlation between predicted value and the calculated value of GABA concentration level and the minimized Mean Squared Error (MSE) also calculated which implies high accuracy. The prediction models based on SBR values for estimating GABA concentration level is a novel method, which overcomes misdiagnoses of early PD.

5. References

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