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Vocal Cord Measures Based Artificial Neural Network Approach for Prediction of Parkinson's Disease Status

Parkinson Hastalığı Seviyesi Tahmininde Vokal Kord Ölçümü Tabanlı Yapay Sinir Ağı Yaklaşımı

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Abstract

Objective: Parkinson's disease is a chronic neurodegenerative impairment which causes movement impairment. Dopaminergic deficiency resulted from the loss of dopaminergic neurons in the substantia nigra causes the disease. UPDRS (Unified Parkinson's disease rating scale) is an important scale for evaluation of clinical severity of Parkinson's disease. Recent computational studies using in silico prediction methods show promising results in terms of their potential diagnostic relevance. This study aims to evaluate the diagnostic potential of in silico methods using vocal cord vibrations and the UPDR scale of Parkinson's Disease for obtaining more precise diagnosis model.

Material-Method: In this study an in silico prediction model using telemonitoring measures, clinical motor and total UPDRS for diagnosis of Parkinson's disease was developed by using regression analysis with neural network model. In addition, we investigated the importance of different attributes in our regression algorithm provided from telemonitoring and UPDRS for evaluation of their predictive relevance.

Results: The correlation between predicted motor UPDRS score and clinical motor UPDRS score was found as 97%. Exclusion of Jitter values did not directly affect the predictive power of the model.

Conclusions: Clinical UPDRS scoring proved its importance to achieve to generate more predictive models.

Keywords: Parkinson's Disease, Artificial Neural Network, Regression Analysis

Özet

Amaç: Parkinson hastalığı kronik, ilerleyici ve nörolojik dejeneratif hareket bozukluğuna sebebiyet veren bir hastalıktır. Dopaminerjik yetersizlik, beyinde substantia nigra bölgesinin pars compacta kısmında dopaminerjik nöronların ölümü sonucu oluşur ve Parkinson hastalığına neden olur. BPHDÖ (Birleşik Parkinson Hastalığı Derecelendirme Ölçeği) Parkinson hastalığının klinik seyrini ölçmede kullanılan en yaygın ölçektir. Siliko tahmin yöntemlerinde kullanılan hesaplamaya dayalı son çalışmalar, tanısal uygulamalarla ilişkileri açısından umut vadetmektedirler. Çalışmada hesaplamalı metodların, vocal kord titreşimleri ölçümü (Telemonitoring) sonuçları kullanılarak Parkinson tanısında kullanılan BPHD ölçeği değerlendirilmesi amaçlanmıştır.

Materyal-Method: Bu çalışmada yapay sinir ağı modeli yardımıyla regresyon analizi yöntemi kullanılarak motor, toplam BPHDÖ klinik sonuçları ve vocal kord ölçümleri kullanılarak Parkinson Hastalığı için tanısal bir model elde edilmeye çalışılmıştır. Buna ek olarak telemonitoring very setinden elde edilen regresyon algoritmasındaki ve BPHD ölçeğindeki farklı niceliklerin önemi araştırılmıştır.

Bulgular: Analiz sonucunda öngörülen BPHDÖ motor sonucu ile klinik ortamda değerlendirilen BPHDÖ motor sonuçları arasındaki korelasyon değeri %97 bulunmuştur. Telemonitoring değerlerinden olan, Jitter değerlerinin regresyon algoritmasından çıkarılmasının, modelin öngörü gücüne doğrudan etkisinin olmadığı görülmüştür.

Sonuç: Oluşturulan tahmin modellerinden elde edilen sonuçlar doğrultusunda, klinik BPHDÖ ölçümlerinin önemi ispatlanmıştır, telemonitoring eklenmesi ile daha iyi bir öngörü modeli oluşturulmuştur.

Anahtar kelimeler: Parkinson Hastalığı, Yapay Sinir Ağları, Regresyon Analizi

Introduction

Parkinson's disease, important neurodegenerative movement impairment, is a progressive and chronic disorder. English medical scientist James Parkinson found the disorder which after then was described as 'vibratile paralysis' (1). It is seen in 2% of the population over 65 years of age. It could not be diagnosed at early stages because of the slow progression. The early symptoms are generally resulted from enteric nervous system and lower brain stem. Cells at substantia nigra produce dopamin hormone. Dopamin is the major chemical substance transmitting message between substantia nigra and other areas inthe brain where responsible for controlling movement of body. Reduction of the cells responsible for dopamin production result to Parkinson's disease's motor symptoms (2).

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Evaluation of clinical severity of Parkinson's disease, Unified Parkinson's disease rating scale (UPDRS) is mostly used as the major scale. The UPDRS is consisted of three components; Behavior, mentation, mood which are major subjects for the scale (3).

Motor UPDRS ranges from 0-108, with 0 representing to free of symptom and 108 to severe motor deficit, and it also uses tremor, speech, facial expression and rigidity. Tsanas et al. reported a method that computes speech signal processing algorithms (4). Tsanas et al. has demonstrated an alignment between UPDRS and dysphonia measures. The association of the measures with total UPDRS and motor functions were demonstrated, using nonlinear and linear regression methods and a classification and regression tree (CART) method. In another study, Marius Ene et. al., 2008 proposed a successful classification model within healthy people and Parkinson's group through probabilistic neural networks by using telemonitoring analysis data set. It was shown that logarithmic transformation of the readings of dysphonia can significantly alter the identification potential forsmall changes in Parkinson's disorder symptoms. The log transformed measures showed superiority in feature selection attempts using Bayesian Least Absolute Shrinkage and Selection Operator (LASSO) linear regression (4).

In this study we aimed to demonstrate a prediction method for evaluation of clinical motor and total UPDRS using regression analysis with neural network. In addition, we investigated the importance of different attributes used in our regression algorithm for evaluation of their predictive relevance. We investigated whether some attributes could predict UPDRS without clinical data for evaluation the predictive efficiency of these attributes. Parkinson's telemonitoring data set is composed of voice measurements from 42 people with early stage Parkinson's disease. Data set attributes are; test time, sex, age, motor UPDRS (clinical score), total UPDRS (clinical score), 5 Jitter values, 6 shimmer values, RPDE, NHR, HNR, PPE and DFA. Exclusion of some attributes from the training data used for the regression model was done and results were examined by correlation scores between predicted and present UPDRS scores in order to show importance of different attributes.

Material-Method

Patients

Telemonitoring measures were obtained from previous study conducted by Goetz et al. (5). According to the data, 52 idiopathic Parkinson's disease subjects were evaluated. At least two of the following symptoms were used for selection of the subjects: rest tremor, bradykinesia, or rigidity, without evidence of other forms of Parkinsonism.

Model Selection: Linear Regression Neural Network

We applied linear regression model by using ANN (Artificial neural network) to telemonitoring data set to predict clinical Parkinson's disease evaluation scale, UPDRS (4). Telemonitoring is a simple voice analysis method that can offer precise evaluation of voice from vocal cord vibrations (6). A simple linear regression line has an equation of $Y=\alpha+\beta X$, where X is the descriptor and Y is the dependent variable, 'β' is the slope, and 'α' is the intercept. However, this investigation required multiple linear regressions. Computer aided diagnosis with artificial neural networks can be employed to various types of imaging, clinical and biochemical data obtained from hospital records. Computer aided mathematical algorithms can classify different types of medical data and turn them into categorized outputs (7).

Neural Network architecture;

In Figure 1, each layer of nodes has inputs from previous layers. The outputs of nodes in one layer are inputs to the next. The inputs to each node to gather uses weighted linear combination. The inputs in hidden neuron j in Figure 1 are linearly combined to give below;

$z_i=b_i+\sum_{i=1}^{4}=w_{ii}\chi_i.$

In the hidden layer, this is then modified using a nonlinear function such as a sigmoid below;

$s(z)=1/(1+e^{(-z)})$

This equation representing to tendency is used to reduce the effect of extreme input values, gives the input for the next layer b1, b2, b3, and w1, w2, w3 … are learned from data.

In this study, computer aided neural network based prediction model using telemonitoring measures, clinical motor and total UPDRS for evaluation of Parkinson's disease was established. We investigated the importance of different attributes with our algorithm for evaluation of their predictive relevance. The regression method has been applied by using RapidMiner 7.0 data mining software (8).

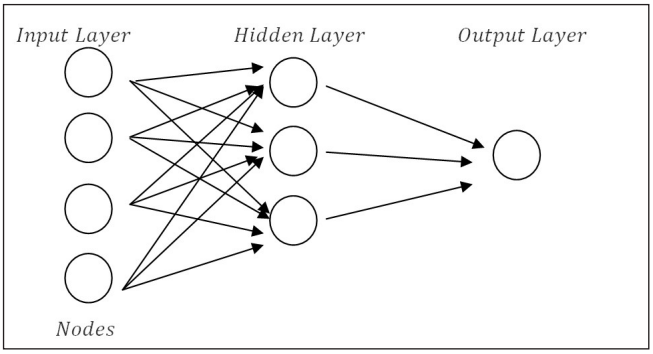

Figure 1. Multilayer feed-forward network

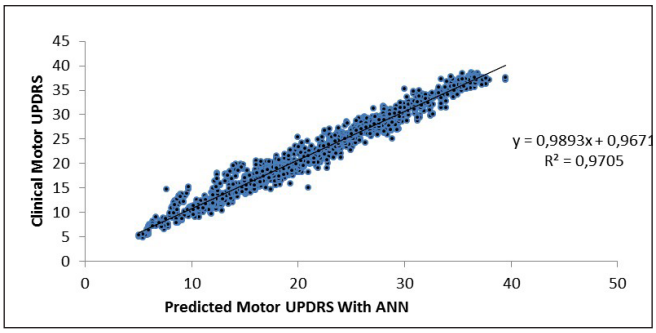

Figure 2. Correlation of clinical and predicted motor

Results

In order to predict motor UPDRS and total UPDRS, important clinical scales in Parkinson's disease, we used neural network model for linear regression analysis. We analyzed six different measurements within three data set. Firstly, motor UPDRS score was predicted with %97 correlation with clinical measurements by the means of neural network regression analysis (Figure 2). Test time, sex, age, Jitter (%), total UPDRS, Jitter: RAP, Jitter (Abs), Jitter: PPQ5, Shimmer, Jitter: DDP, Shimmer: APQ5, Shimmer (dB), Shimmer: APQ11, Shimmer: DDA, Shimmer: APQ3, NHR, RPDE, DFA, HNR and PPE were selected as training attributes. Consequently, we excluded total UPDRS attribute from training data set, and analysis was repeated. Accordingly, correlation of predicted motor UPDRS and clinical motor UPDRS was shown to be reduced to 72% (Figure 3). Therefore, results demonstrated the importance of clinical evaluation to achieve more vigorous predictive models. Exclusion of clinical data clearly impairs the predictive capability of the model up to 20%. Use of motor UPDRS and total UPDRS together with other attributes clearly increases the predictive power.

Total UPDRS score was predicted with 97% correlation when motor UPDRS clinical measurements were used in the training data set (Figure 4). When we excluded the motor UPDRS attribute from training set, total UPDRS prediction efficiency reduced up to 76% (Figure 5). Just as we see the decreased predictive power of the regression model when we exclude motor UPDRS scores from training set while we predict total UPDRS scores, predictive power of the model reduced up to 21% for prediction of total UPDRS when we exclude motor UPDRS scores from training data set. Thus, clinical measurements once more proved their importance to achieve to generate more predictive models. Another important point is that motor UPDRS and total UPDRS scores have similar importance in terms of their predictive relevance.

After that, we excluded all Jitter values from training data set and predicted motor UPDRS scores. The correlation between predicted motor UPDRS score and clinical motor UPDRS score was found as 97% (Figure 6). Accordingly, exclusion of Jitter values did not directly affect the predictive power of the model, so that Jitter values can be excluded for the future prediction attempts.

Afterwards we removed Jitter values and total UPDRS scores together and predicted motor UPDRS scores. The correlation between predicted and clinical motor UPDRS score was found as 79% (Figure 7). Once more it is seen that clinical evaluations should be done and absolutely added to training data set in order to generate more powerful predictive models.

Discussion

Motor UPDRS score was predicted with high accuracy by using attributes involving test time, sex, age, Jitter (%), total UPDRS, Jitter: RAP, Jitter (Abs), Jitter: PPQ5, Shimmer, Jitter: DDP, Shimmer: APQ5, Shimmer (dB), Shimmer: APQ11, Shimmer: DDA, Shimmer: APQ3, NHR, RPDE, DFA, HNR and PPE (Figure 2). Exclusion of total UPDRS

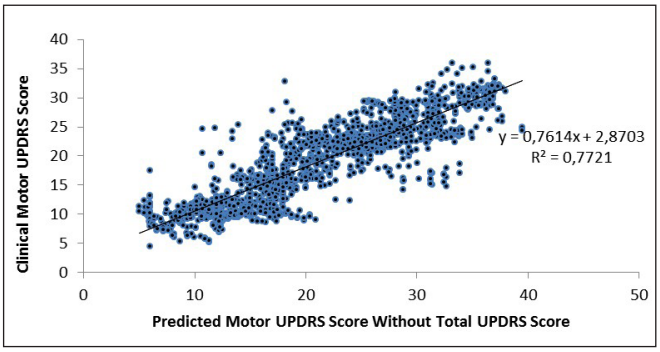

Figure 3. Correlation of clinical and predicted motor UPDRS without total UPDRS

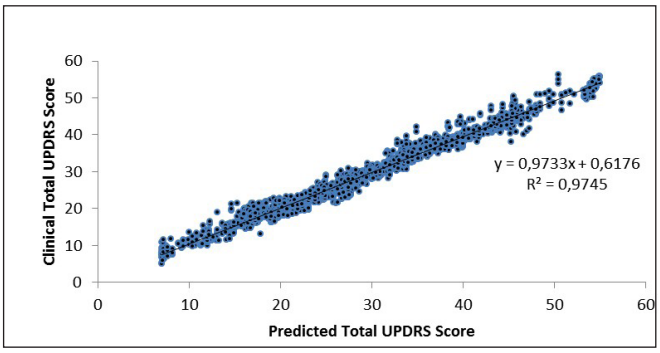

Figure 4. Correlation of clinical and predicted total UPDRS

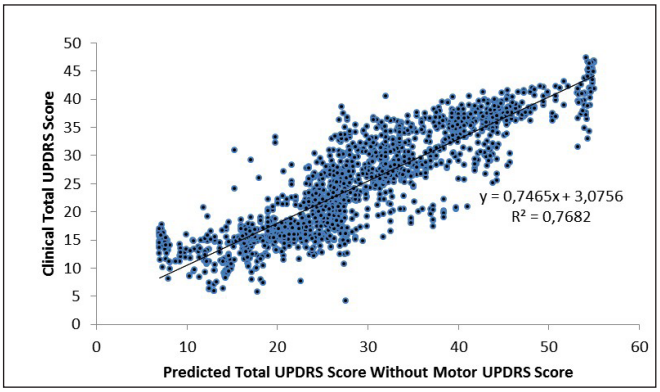

Figure 5. Correlation of clinical and predicted total UPDRS score without motor UPDRS

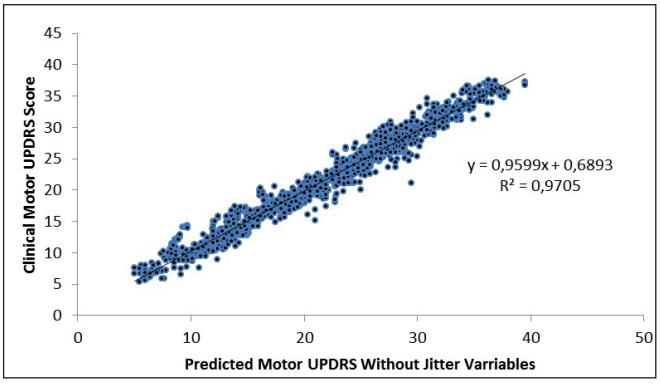

Figure 6. Correlation of clinical and predicted motor UPDRS score without Jitter variables

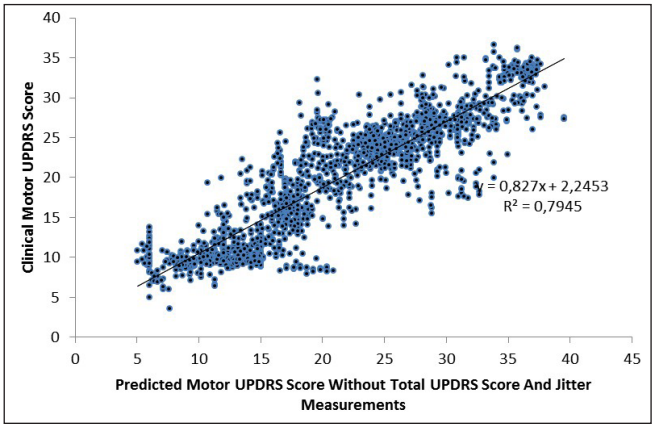

Figure 7. Correlation of clinical and predicted motor UPDRS score without Jitter variables and total UPDRS

attribute from training set, and analysis was repeated. Correlation of predicted motor UPDRS and clinical motor UPDRS was shown to be reduced to 72% (Figure 3). This suggests motor UPDRS measures are highly correlated with total UPDRS score. Evaluation of secondary motor deficits play important role in diagnosis of Parkinson's disease (9). Therefore, lower accuracy of prediction is resulted when total UPDRS is excluded from training attributes. In order to demonstrate strong association between motor UPDRS and total UPDRS scores, we then excluded motor UPDRS score from attributes when predicting total UPDRS score. Once more, motor UPDRS proved its importance in diagnosis in Parkinson's disease.

After exclusion of Jitter values from training attributes. The correlation between predicted motor UPDRS score and actual motor UPDRS score was found as 97% (Figure 6). Exclusion of Jitter values did not directly affect the predictive power of the model, so that it can be suggested that Jitter values are not enough to predict motor UPDRS with high accuracy without clinical evaluation by using UPDRS. But including Jitter values obtained from telemonitoring would indeed increase the prediction power which might be useful in early diagnosis of Parkinson's disease.

In this study we demonstrated the importance of different predictive attributes as biomarkers for potential early diagnosis of Parkinson's disease. Clinical evaluation scores were shown to be utmost important for achieving more accurate and robust prediction models. Different variables might be added to training features so that the potential of predictive model might be improved for the clinical diagnosis of the disease.

Acknowledgements

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Abbreviations

UPDRS: Unified Parkinson's disease rating scale

CART: Classification and regression tree

LASSO: Least absolute shrinkage and selection operator

RPDE: Recurrence period density entropy

DFA: Detrended fluctuation analysis

PPE: Pitch period entropy

HNR: Harmonics to noise ratio

NHR: Noise to harmonics ratio

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