AMERICAN SCIENTIFIC PUBLISHERS

Journal of Medical Imaging and Health Informatics
Vol. 5, 1358–1363, 2015

Diagnosis of Parkinson's Disease Using Speech Samples and Threshold-Based Classification

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In this paper we investigate the diagnosis of Parkinson's disease on the basis of characteristic features of a person's voice. First, the individual voice samples are classified as belonging either to a sick or to a healthy person. For that task, decision trees (the most efficient classifier) are selected. Second, using the threshold-based method, the final diagnosis of a person is made using previously classified voice samples. The value of the threshold determines the minimal number of individual voice samples (indicating the disease) that is required for the reliable diagnosis of a sick person. After numerous experiments with real-world data, the accuracy of classification achieved 90%. The high efficiency of diagnosis justifies that the proposed approach is worth using in medical practice.

Keywords: Parkinson's Disease, Medical Diagnosis, Data Classification.

1. INTRODUCTION

This paper addresses the important problem of early diagnosis of Parkinson's disease.[16] Parkinson's disease is a disorder of the central nervous system and leads to many health issues, e.g., rigidity, imbalance, difficulty talking, and slowness of movement. It is estimated that seven to ten million people worldwide currently suffer from Parkinson's disease. Parkinson's disease also manifests in the form of speech disorders. Therefore, it is possible to diagnose Parkinson's disease using voice signals.[28,30] A medical background related to the disease is presented in Section 2.

In general, medical diagnosis support is a challenge that is considered in many studies.[9–11,26] The problem of early diagnosis of Parkinson's disease especially has piqued the interest of numerous researchers.[4,6,19] In particular, the application of artificial neural networks to discriminate healthy people from those with Parkinson's disease using voice signals was proposed.[6] Parkinson's disease classification using gait characteristics and wavelet-based feature extraction was proposed.[19] Application of a fuzzy *k*-nearest neighbor model for an efficient detection of Parkinson's disease was proposed.[4]

Recently, a hybrid system based on model-based clustering and classification using support vector machine and artificial neural networks has been proposed.[14] Comparative experiments with different classifiers applied to the diagnosis of Parkinson's disease using voice signals has been made.[28] A literature overview on signal processing algorithms for the classification of Parkinson's disease is available.[32]

There are several limitations in the existing studies. To the best of our knowledge, all existing approaches deal with the problem of classifying individual voice samples and do not take into account the distribution of those samples and their classes with respect to persons. Moreover, the existing studies do not consider that the voice samples coming from a particular person can be correlated with each other. For those reasons, even if the obtained classification accuracy of all voice samples in their entire population is high, [4,14] the accuracy obtained for diagnosing individual patients remains unknown. In the case of an unbalanced distribution of samples and their classes with respect to persons the final accuracy of diagnosis may be much lower than that for all samples. Also, in many of the existing studies, 10-fold or 5-fold cross validation tests were performed using the data sets of hundreds of samples. However, after assigning those numerous samples to persons, it may turn out that the number of persons is too low to use those types of validations with respect to persons.

In this paper we address the aforementioned limitations. Our study proposes a new two-step classification approach. In the first step, the voice samples are classified using standard state-of-the-art classifiers. In the second step, the classified samples are assigned to patients and the final classification process is performed. This study is an substantial extension of our previous work.[12] In addition, we propose using decision trees that have been recognized as the most effective classifier during the first step of the investigated approach. In the second step, we formerly used a simple majority criterion for the final classification. Instead, we now propose a fine-tuned threshold-based criterion that leads to better classification accuracy. Moreover, the currently proposed classification criterion overcomes the previously

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 2156-7018/2015/5/1358/006 doi:10.1166/jmihi.2015.1539

encountered problem of ambiguity in cases when the numbers of voice samples indicating sick and healthy persons were equal. In addition to our previous work, medical background and the applied characteristic features of the voice are described in detail.

All experiments in this paper have been performed using publicly available real-world data that play the role of an established standard for benchmarking the classification of voice samples.[21] However, due to the completely new, two-step diagnosing procedure proposed in this paper that is performed with respect to persons, the obtained results are not comparable to those known from the literature that are related only to individual voice samples.

The remainder of this paper is organized in the following way: the medical background of Parkinson's disease is presented in Section 2; in Section 3, the proposed two-step, threshold-based approach to the medical diagnosis is proposed; the description of the applied data and the results of experiments are presented in Section 4; Section 5 concludes the paper.

2. MEDICAL BACKGROUND

Parkinson's disease (PD) was named after the doctor James Parkinson who described it for the first time in 1817.[23] However, the disease had been known much earlier as paralysis agitans. The name "Parkinson's disease" was introduced by the French physician Jean-Martin Charcot, who investigated it from 1868 to 1881.[20] In subsequent years, many scientists and doctors conducted research on Parkinson's disease. In 1960, Ehringer and Hornykiewicz tried to explain the pathogenesis of the disease in their study.[15] In turn, the Swedish scientist Arvid Carlsson presented biochemical changes underlying the disease.[3] For this discovery he was awarded the Nobel Prize in 2000.

PD is a spontaneous, slowly progressing disorder of the central nervous system; it is one of the extrapyramidal system disorders.[13] This disorder includes the degeneration of nerve cells in certain parts of the brain, inter alia in the substantia nigra. The effects of this degeneration may include visible and noticeable symptoms. The most characteristic symptoms are as follows: shaking, muscle stiffness, rigidity, and slow movements. Other basic symptoms include the inability to maintain balance and problems with speech and walking. The classification of PD symptoms has been made.[13] The symptoms were divided into initial, primary and secondary, as well as those associated with treatment of the disease and those related to the mood and behaviour of a patient.

The exact cause of the cell degeneration in PD is not currently known. The literature describes different reasons, including genetic and hereditary conditions, environmental impact and improper lifestyle and nutrition.[13] In turn it is known that symptoms of PD are caused by necrosis of the brain cells that form the chemical compound called dopamine.[13] Therefore, the most common medicine administered in the early stages of the treatment of Parkinson's disease is L-DOPA,[22] which is a metabolic precursor of dopamine. While this medicine does not cause recovery of the lost cells, it stimulates the remaining cells to produce more dopamine, which helps compensate for the loss. In the advanced stages of PD, treatment with this medicine has no effect. The loss of cells is so large that the remaining cells cannot keep up with the production of dopamine, despite the administration of this medicine.[13,22]

PD is a chronic and usually slowly progressing disease. However, both the progress rate and the symptoms of the disease may be different depending on the person. In some people, the course of the disease is very mild for many years, while in others disability progresses very quickly. PD occurs in similar proportions in females and males world-wide. It is estimated that seven to ten million people around the world currently suffer from PD. Initial symptoms may appear at any age; however, they rarely occur in people before forty years of age and very rarely in people before twenty years of age. In general, these symptoms appear between sixty and seventy years of age. The average age of PD occurrence is approximately 59 years.[13]

Unfortunately there are no medicines for PD that can slow down or stop the disease. The aforementioned L-DOPA has an effect only in the initial stages of the disease. In addition, it has been found that medicines based on artificial dopamine have side effects.[1,17] Therefore, treatment consists of suppression or reduction of symptoms and medicines are selected individually by a doctor depending on the condition of the patient. It is also advisable to have a diet that involves avoiding certain food items and doing regular gymnastics.[13] Surgery is indicated in rare cases. There is also a large number of procedures that may improve the quality of life for people with PD, potentially for a long time.

Currently, there are neither radiologic examinations nor blood tests dedicated to diagnosing PD. The diagnosis of PD is based only on the patient's medical history and clinical examination performed by a doctor.[13] Because symptoms of PD include speech disorders, it is possible to diagnose the disease with the use of voice signals. On the basis of the patient's voice sample, numerical data defining the characteristic feature of the recorded voice are generated. Based on these data, it is possible to determine whether a given person shows adequate symptoms of the disease.

Gathering voice samples and research on the diagnosis of PD using those samples was always performed with the cooperation of doctors, experts on signal analysis, and researchers from the computer science domain. For example, contributions have been made by the following: Georgia Institute of Technology, National Institutes of Health, Oregon Health and Science University, Rush University Medical Center, Southern Illinois University, and University of California.[7] Similar work has also been supported in Spain by the Ministry of Health.[8]

Intel Corporation developed a testing device that facilitates remote, non-invasive, self-administered tests specifically designed to track PD progression.[31] The objective was to apply the obtained methods during the therapy of patients in hospitals or at homes.

3. TWO-STEP CLASSIFICATION PROCEDURE

Let $P = \{P_1, P_2, \ldots, P_n\}$ be a set of persons, where $n = \mathrm{card}(P)$ is its cardinality. For every person P_i, the classification $d_i \in K$ should be made where K is the assumed set of classes. For our purpose $K = \{0, 1\}$ where 0 denotes a healthy person and 1 indicates that the patient suffers from Parkinson's disease. This way, the value of d_i determines medical diagnosis. In the case that the diagnosis is predicted by our method, we will denote it as d_i'.

The classification error for the ith patient can be calculated from the following formula:

$$e_i = |d_i^{'} - d_i| \tag{1}$$

To every person P_i a set of characteristic vectors S_i is assigned. Let $S = \{S_1, S_2, \ldots, S_n\}$ be the set of characteristic vectors collected for all persons, where: $\mathrm{card}(S) = \sum_{i=1}^{n} \mathrm{card}(S_i)$.

It is assumed that for any person P_i, the value of $d_i^{'}$ is calculated on the basis of the collected voice samples. For every such sample, a vector of characteristic features is calculated. Let us denote a single characteristic vector as $s_{ij} \in S_i$, where the subscripts i, j denote the index of the person and the index of the characteristic vector respectively. Let us denote $d_{ij} \in K$ as the classification of that vector. To perform a diagnosis for the person P_i the following two-step classification procedure is proposed.

3.1. First Step of the Classification Procedure

In the first step, for every characteristic vector $s_{ij} \in S_i$, a binary classification reflecting the severity of the Parkinson's disease is assigned. The classification is made using the following formula:

$$d_{ij}^{'} = M(s_{ij}) \tag{2}$$

where M denotes a model (classifier) trained on the basis of historical data. It is assumed that the same classifier M is used for all characteristic vectors of all persons. We will say that the characteristic vector s_{ij} supports the class $k \in K$, when its classification is equal to k, i.e., $d_{ij}^{'} = k$. In the experimental part of the paper we select the most effective state-of-the-art classifier to play the role of model M.

To perform the final diagnosis for the considered person P_i, it is necessary to calculate the value of $d_i^{'}$ using the set of previously calculated $d_{ij}^{'}$ for all $j = 1, 2, \ldots, \mathrm{card}(S_i)$. This task is performed in the second step of the proposed procedure.

3.2. Second Step of the Classification Procedure

Let us calculate the number $\mathrm{supp}_i(k)$ of characteristic vectors supporting each of the possible classes $k \in K$ for a given ith person. For the class of sick persons, i.e., for $k = 1$ we define its support as follows:

$$\mathrm{supp}_i(1) = \sum_{j=1}^{\mathrm{card}(S_i)} d_{ij}^{'} \tag{3}$$

For the rest of vectors indicating the healthy person, i.e., for $k = 0$ the support is calculated by means of the following formula:

$$\mathrm{supp}_i(0) = \mathrm{card}(S_i) - \mathrm{supp}_i(1) \tag{4}$$

Let us define now the rate of samples indicating the occurrence of the disease with respect to all samples available for a given person:

$$\alpha_i(k) = \frac{\mathrm{supp}_i(k)}{\mathrm{card}(S_i)} \tag{5}$$

For the final medical diagnosis, we propose the application of the following criterion:

$$d_i^{'} = \begin{cases} 1 & \text{if } \alpha_i(1) > \tau \\ 0 & \text{if } \alpha_i(1) \leq \tau \end{cases} \tag{6}$$

The parameter $\tau \in [0, 1]$ is a threshold imposed on the rate of samples supporting the occurrence of Parkinson's disease. It determines in fact a discrimination point between healthy and sick persons. In cases when the value of $\alpha_i(1)$ is above τ, the final diagnosis is made that the given person is sick; otherwise the person is classified as healthy. It is worth noting here that contrary our previous work,[12] there is no requirement that the majority of voice samples must indicate the disease. The threshold τ will be adjusted experimentally dependent on the accuracy of classification achieved by a given classifier M.

Table I. Characteristic features of voice samples.

Feature	Description
MDVP:Fo (Hz)	Average fundamental frequency for the vocalization.
MDVP:Fhi (Hz)	Maximum vocal fundamental frequency.
MDVP:Flo (Hz)	Minimum vocal fundamental frequency.
MDVP:Jitter (%)	Jitter percent represents the relative period-to-period (in short-term) variability of the pitch.
MDVP:Jitter Abs (ms)	Absolute jitter gives an evaluation of the period-to-period variability of the pitch period.
MDVP:RAP (%)	Relative average perturbation gives the variability of the pitch period with a smoothing factor of three periods.
MDVP:PPQ (%)	Pitch period perturbation quotient gives the variability of the pitch period with a smoothing factor of 5 periods.
Jitter:DDP	Average absolute difference of differences between cycles, divided by the average period.
MDVP:Shimmer (%)	Shimmer percent gives the variability of the peak-to-peak amplitude. It represents the relative period-to-period (in short-term) variability of the peak-to-peak amplitude.
MDVP:Shimmer (dB)	Shimmer in dB gives the period-to-period variability of the peak-to-peak amplitude within the analysed voice sample.
Shimmer:APQ3	Three point amplitude perturbation quotient.
Shimmer:APQ5	Five point amplitude perturbation quotient.
MDVP:APQ (%)	Amplitude perturbation quotient gives the variability of the peak-to-peak amplitude with a smoothing factor of 11 periods.
Shimmer:DDA	Average absolute difference between consecutive differences between the amplitudes of consecutive periods.
NHR (%)	Noise-to-harmonics ratio.
HNR (dB)	Harmonics-to-noise ratio.
RPDE	Recurrence period density entropy.
D2	Correlation dimension.
DFA	Detrended fluctuation analysis.
spread1	Non linear measure of fundamental frequency.
spread2	Non linear measure of fundamental frequency.
PPE	Pitch period entropy.

4. EXPERIMENTAL DETAILS

For the experiments, real-world data from the UCI repository were used.[21] The voice samples were gathered from persons aged 46 to 85 years. The time since their disease diagnosis ranged from 0 to 28 years. For the recordings, an AKG C420 microphone fitted on the head, 8 cm from the mouth was used. The microphone was calibrated using sound level meter B&K 2238. The patients pronounced a vowel sound for as long as they could. The signal was sent to the computer using CSL 4300B hardware (KayElemetrics) and sampled at a rate of 44.1 kHz with a 16-bit resolution. The researchers who assisted the recordings were blind to the diagnosis. The final diagnosis of the disease was made by experienced physicians.

As mentioned in the introduction, in spite of the limited number of samples, the selected set of data is usually used for benchmarking. However, the two-step approach was investigated for the first time. Therefore, the results of classification accuracy presented in this paper are related to persons, not individual voice samples. They therefore are not comparable to those available in the literature.

4.1. Source Data

There are 24 attributes in the considered data set. A single attribute contains a symbol that is a person's identifier. The other binary attribute signifies the class to which the characteristic vector is classified. The number of real valued characteristic features of a voice sample and the dimension of space in which the classification is made is equal to 22. The description of characteristic features selected from the Multi Dimensional Voice Program (MDVP) is given in Table I.

The data file contains card$(S) = 195$ characteristic vectors, wherein 147 of them are assigned to sick persons and 48 to healthy persons. The distribution of classes among characteristic vectors is 0.7538/0.2462.

The characteristic vectors are not equally distributed among persons with respect to their number and with respect to their classes. To the majority of patients, 6 characteristic vectors are assigned with the exception of patients identified as S_{21}, S_{27}, and S_{35} to whom 7 vectors are assigned. Among 32 persons for which the data were recorded, 24 are sick and 8 are healthy. This means that the distribution of classes among persons is: 0.75/0.25.

4.2. Accuracy of Classification

For the first step of our approach, we performed experiments with numerous state-of-the-art classifiers playing the role of the model M. Here we present only the results achieved by the most effective of them: k-nearest neighbour (kNN) lazy classifier, naive Bayesian (NB) statistical classifier, artificial neural networks (ANN) blackbox classifier, fuzzy rule-based system (FRBS), support vector machine (SVM), and the decision tree (DT) classifier. Every one of the considered classifiers required the selection of its learning algorithm and the adjusting of its specific parameters. This task was performed on a trial-and-error basis in numerous experiments. In cases when the obtained accuracy for different learning algorithms or parameters resulted in the same or very similar results, those leading to shorter execution times were selected. The description regarding the experimental setup is given in Table II.

Table II. Experimental setup.

Classifier	Description
kNN	$k = 10$, neighbors were weighted by distance.[25]
NB	Gaussian distribution for numerical attributes, euclidean distance applied.
ANN	A single hidden layer with 50 neurons. RProp training algorithm for multilayer feed-forward network.[27] Maximum number of iterations:100.
FRBS	Mixed fuzzy rule formation as the training algorithm,[2] min/max norm.
SVM	Support vector machine learning algorithm,[24] polynomial kernel.
DT	Gini index as a quality measure, no pruning, learning algorithm.[29]

Table III. Percentage of persons with an equal number of samples supporting both classes.

kNN	NB	ANN	FRBS	SVM	DT
12.5%	9.375%	6.25%	3.125%	6.25%	3.125%

At the preliminary stage of the validation of our method, we decided to check the percentage of persons for which the selected classifiers produced (in the first step of the proposed procedure) equal numbers of vectors supporting both classes (healthy and sick persons). In such a case, the intuitive decision regarding the diagnosis is ambiguous. The obtained number differed depending on the selected classifier.

The results given in Table III raise a question that is addressed during further experiments, i.e., what is the minimal number of characteristic vectors indicating the occurrence of disease that justifies the final diagnosis? The question is formally equivalent to the selection of the minimal value of threshold assuring the best possible accuracy of diagnosis. Taking into account different reliability of classifiers confirmed by the results given in Table III, the following experiment was designed.

To select the value of τ and validate our method the Leave-One-Out Cross Validation (LOOCV) was performed.[5] The resulting accuracies, dependent on $\alpha_i(1)$, are given in Table IV. As can be noted, the reliability of the diagnosis differs for every one of the classifiers. In the first step of our approach, the winning classification method is based on decision trees. To a certain extent, a surprising phenomenon can be observed in Table IV. The high increase of τ is not beneficial; imposing the requirement of a high τ makes the number of patients diagnosed as sick lower. On the other hand, setting τ too low classifies more healthy persons as sick. In both cases, the rate of the correct diagnoses decreases. For the above reason, the optimal value of τ is placed within a

Table IV. Classification results.

τ	kNN	NB	ANN	FRBS	SVM	DT
0.1	0.78125	0.75000	0.75000	0.78125	0.78100	0.87500
0.2	**0.81250**	0.78125	0.65625	**0.84375**	**0.81250**	**0.90625**
0.3	**0.81250**	0.78125	0.65625	**0.84375**	**0.81250**	**0.90625**
0.4	**0.81250**	**0.84375**	0.65625	0.81250	0.78100	**0.90625**
0.5	0.75000	0.75000	0.71785	0.81250	0.78100	0.87500
0.6	0.75000	0.75000	0.71785	0.81250	0.78100	0.87500
0.7	0.71875	0.68750	**0.81250**	0.81250	0.78100	0.84375
0.8	0.71875	0.68750	0.78100	0.78125	0.78100	0.84375
0.9	0.68750	0.65625	0.68750	0.71875	0.78100	0.75000
1.0	0.68750	0.65625	0.68750	0.71875	0.78100	0.75000

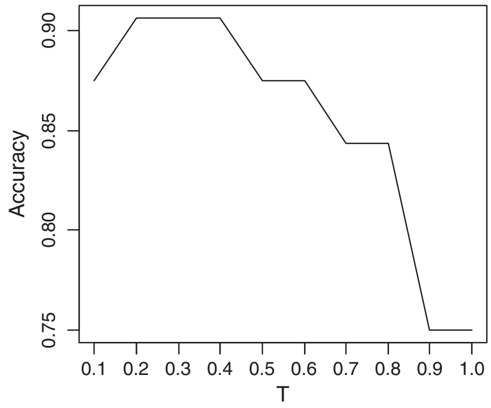

Fig. 1. Accuracy of the classification using decision trees.

certain range. The observed effect for the winning decision tree classifier is depicted in Figure 1.

Two conclusions are drawn from the performed experiment:

1. The decision tree model should be used to classify individual voice samples.
2. The threshold value for the final medical diagnosis should be set in the range $\tau \in [0.2, 0.4]$. The final decision regarding the value of τ should be made by the doctor, taking into account all possible medical consequences. Higher τ increases the risk of classifying a sick person as healthy; lower τ leads to the opposite effect.

To finalize our experimental investigations we provide in Table V the confusion matrix for LOOCV of the winning decision tree model and the threshold $\tau = 0.2$. It is important to note that only one sick person from the population of 32 was wrongly classified as healthy. In our opinion, the medical consequences following two misclassified healthy people are lower.

All experiments described in this section were implemented using the KNIME experimentation platform[18] with the support of nodes implemented in Java.

5. FINAL REMARKS

In this paper a new two-step, threshold-based approach for the classification of voice samples with respect to patients has been proposed. The classification enables efficient diagnosing of Parkinson's disease. In the first step of the pro-posed approach every individual voice sample is classified. In the second step, on the basis of already classified samples, a final medical diagnosis of a person is made. The performed experiments provide evidence for the high accuracy of the proposed method. The recommended directions for further research involve the application of more advanced methods for the selection of parameters of all applied models. Also, validation of our method using more data would be beneficial.

Table V. Confusion matrix for the decision trees.

		Predicted class	
		1	0
Real class	1	23	1
	0	2	6

Acknowledgment: This work was supported by the Polish National Science Centre under the grant no. DEC-2013/09/B/ST6/02264.

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Received: 17 November 2014. Revised/Accepted: 23 March 2015.