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Comparison among probabilistic neural network, support vector machine and logistic regression for evaluating the effect of subthalamic stimulation in Parkinson disease on ground reaction force during gait

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ABSTRACT

Deep brain stimulation of the subthalamic nucleus (DBS-STN) is an approved treatment for advanced Parkinson disease (PD) patients; however, there is a need to further evaluate its effect on gait. This study compares logistic regression (LR), probabilistic neural network (PNN) and support vector machine (SVM) classifiers for discriminating between normal and PD subjects in assessing the effects of DBS-STN on ground reaction force (GRF) with and without medication. Gait analysis of 45 subjects (30 normal and 15 PD subjects who underwent bilateral DBS-STN) was performed. PD subjects were assessed under four test conditions: without treatment (mof-sof), with stimulation alone (mof-son), with medication alone (mon-sof), and with medication and stimulation (mon-son). Principal component (PC) analysis was applied to the three components of GRF separately, where six PC scores from vertical, one from anterior–posterior and one from medial–lateral were chosen by the broken stick test. Stepwise LR analysis employed the first two and fifth vertical PC scores as input variables. Using the bootstrap approach to compare model performances for classifying GRF patterns from normal and untreated PD subjects, the first three and the fifth vertical PCs were attained as SVM input variables, while the same ones plus the first anterior–posterior were selected as PNN input variables. PNN performed better than LR and SVM according to area under the receiver operating characteristic curve and the negative likelihood ratio. When evaluating treatment effects, the classifiers indicated that DBS-STN alone was more effective than medication alone, but the greatest improvements occurred with both treatments together.

1. Introduction

Parkinson disease (PD) is a neurodegenerative disorder leading to difficulty in motor function, including gait and balance. Deep brain stimulation of the subthalamic nucleus (DBS-STN) is a treatment for advanced PD patients with disabling motor fluctuations, allowing a significant reduction in dopaminergic medications (Ferrarin et al., 2005). Various studies have evaluated the effects of DBS-STN using clinical motor scores (Krack et al., 2003; Ostergaard and Sundae, 2006), while only a few have quantitatively assessed the gait of PD patients (Liu et al., 2005; Ferrarin et al., 2005). Gait speed is shown to be the variable most affected by the DBS-STN; however, it does not take into account atypical waveforms and therefore does not provide enough information about the gait pattern (Schwartz and Rozumalski, 2008). Approaches that capture features of the entire waveform instead of a few parameters may improve the effectiveness of the analysis (Chester et al., 2007). Additionally, the correlations among variables must be considered to accurately evaluate the extent of gait abnormalities and to assess the changes resulting from a specific treatment (Schutte et al., 2000).

A clinical challenge is to understand the disease process as well as outcomes of potential interventions. Logistic regression (LR) is commonly used as a linear predictive model for diagnostic and prognostic tasks. Recently, computational intelligence techniques such as artificial neural networks (ANN) and support vector machines (SVM) have played an important role in gait classification and the diagnosis of diseases (Lai et al., 2009). Studies have compared the predictive ability of LR and ANN (Dreiseitl and Ohno-Machado, 2002; Song et al., 2005). ANN modeling has been used in gait analysis focusing on pattern recognition (Hahn et al., 2005), as well as for classifying normal and pathological patterns (Lafuente et al., 1997; Su and Wu, 2000). SVM has recently been used for automated identification of gait pathologies (Begg et al.,

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2005; Lai et al., 2009). However, none of the past studies compared LR, probabilistic neural network (PNN) and SVM in classifying gait patterns or evaluated the effect of therapeutic interventions on ground reaction force (GRF) of PD patients.

This study evaluated LR, PNN and SVM models for discriminating between normal and PD subjects using principal components derived from the GRF as input variables. For performance evaluation, the accuracies (ACC) and the areas under the receiver operating characteristic (ROC) curves (AUC) based on 1000 bootstrap runs of the classifiers were compared. The effects of DBS-STN on GRF with and without medication were also evaluated with both the models.

2. Materials and methods

2.1. Studied groups

The subjects (n=45) consisted of 30 healthy controls (20 women) and 15 PD patients (three women). The healthy subjects, recruiting by advertisements, were without neurological illness, degenerative conditions or any general disease that might interfere with gait (Table 1). A screening questionnaire was completed to guarantee that subjects were suitable for the study. The PD subjects were recruited from the Parkinson Disease and Movement Disorder Center of the University of Kansas Medical Center. All PD subjects had undergone bilateral DBS-STN and were stable when the study was conducted. Each subject signed an informed consent approved by the local Institutional Review Board.

2.2. Experimental protocol and signal processing

For each PD subject, quantitative gait measurement was obtained on two different days. In the first session, the subject had taken the usual dose of PD medication and stimulators were turned "on". The gait assessment was first conducted with both medication and stimulation (mon-son). After turning the stimulators off for 30 min, the measurements were repeated (mon-sof). In the second session, the subjects were without medication for at least 12 h. Gait analysis was first conducted with stimulation (mof-son), and repeated after 30 min without stimulation (mof-sof). Due to technical problems, some subjects did not complete all tests. Therefore, 13 subjects were evaluated in mof-sof, 12 in mof-son, 14 in mon-sof and 11 in mon-son conditions. Subjects from the control group were evaluated only once. The quantitative analysis for the controls and PD subjects in the mof-sof condition was used to develop the classifier models. The other three PD conditions were included in the developed models to evaluate the DBS-STN effect in PD treatment.

Two force platforms (AMTI, USA) were mounted in series at the middle of a walkway. All subjects practiced the walking trial five times before the experiment. The subjects walked barefoot at their self-selected speed and repeated the walking trial five times. The GRF from both force platforms were collected for 10 s at a sampling frequency of 100 Hz, filtered using a low-pass Butterworth filter, with a cut-off frequency of 30 Hz, and normalized by subject body weight.

The averaged vertical, anterior–posterior and medial–lateral components of GRF from five walking trials were interpolated with cubic splines and re-sampled with 101 sample points according to the stance phase duration of each foot. Thus, 202 GRF samples were analyzed for each GRF component separately.

Each vertical, anterior–posterior and medial–lateral GRF waveform was stored in a matrix **E** with 43 rows (# of subjects) and 202 columns (# of GRF samples for both right and left limbs). Principal component analysis (PCA) was applied to the covariance matrices **S** (202 × 202) from each **E**, separately (Jollife, 2002).

2.3. Logistic regression

LR is a statistical modeling technique that estimates the probability of a dichotomous outcome event being related to a set of explanatory variables (Schumacher et al., 1996):

$$P(x) = \frac{1}{1+e^{-\beta_o + \sum_{i=1}^{n} \beta_i Pc_i}} \quad (1)$$

where β_o is the intercept and β_i is the coefficient associated with the explanatory variable PC_i. The maximum likelihood estimation method is used to estimate the β coefficients. For subjects' classification, the PC scores were selected as the independent variables for computing the natural logarithm of the odds ratio; the ratio between the probabilities that an event will or will not occur (1—controls and 0—PD subjects). The classification threshold was set to 0.5.

2.4. Probabilistic neural networks

PNN is a feedforward ANN developed by Specht (1990), in which the response to an input pattern is processed from one layer to the next, without feedback paths to previous layers. A typical PNN has four layers: input, pattern, summation and output. The input units supply the same values to all pattern units. The pattern units form a dot product between the input pattern vector **x** and a weight vector $\mathbf{w}_i$ ($\mathbf{z}_i$=$\mathbf{x}\mathbf{w}_i$), which is followed by the nonlinear neuron activation function:

$$g(\mathbf{z}_i) = \exp\left[-\frac{(\mathbf{w}_i - \mathbf{x})'(\mathbf{w}_i - \mathbf{x})}{2\sigma^2}\right] \quad [2]$$

This Bayesian function takes into account the relative likelihood of events and uses a priori information to improve the prediction (Specht and Romsdahl, 1994). The summation units simply sum the inputs from the pattern units, corresponding to the category from which the training patterns were selected. Repeating this procedure for each class, the un-normalized density functions g_k (x), for k=1, 2, …, K were estimated. The Bayesian probability that the case was from class k is as follows:

$$P(x \in k) = \frac{g_i(x)}{\sum_{i=1}^{k} g_i(x)} \quad (3)$$

The output units have a competitive transfer function that picks the maximum of the probabilities and produces 1 for one class (normals) and 0 (PD patients) for the other.

2.5. Support vector machine

The SVM estimates a function for classifying data into two classes (Vapnik, 2000). Using a nonlinear transformation Φ that depends on a regularization parameter C (Begg et al., 2005), the input vectors are placed into a high-dimensional feature space, where a linear separation is employed. To construct a nonlinear support vector classifier, the inner product ($\boldsymbol{x}$,$\boldsymbol{y}$) is replaced by a kernel function $K(\boldsymbol{x},\boldsymbol{y})$

$$f(\mathbf{x}) = \operatorname{sgn}\left(\sum_{i=1}^{l} \alpha_i \mathbf{y}_i K(\mathbf{x}_i, \mathbf{x}) + b\right) \quad [4]$$

where $f(\boldsymbol{x})$ determines the membership of $\boldsymbol{x}$. In this study, the normal subjects were labeled as −1 and PD subjects as +1. The SVM has two layers. During the learning process, the first layer selects the basis $K(x_i,\boldsymbol{x})$, i=1,2, …, N from the given set of kernels, while the second layer constructs a linear function in the Φ space. This is equivalent to finding the optimal hyperplane in the corresponding feature space. The SVM algorithm can construct a variety of learning machines using different kernel functions.

2.6. Variable selection

The broken stick criterion (Jolliffe, 2002) was used for choosing the significant PCs of vertical, anterior–posterior and medial–lateral GRF components for the analysis. Moreover, to build a more accurate classifier model, it was necessary to evaluate which scores contributed to improvement in the task (Chang, 1983).

In the LR model, a stepwise approach was used to select the input variables by the Akaike information criterion (AIC), followed by χ^2 tests to contrast with a full model including all PC scores selected by the broken stick criterion or with subsets of variables close to the final model (Krzanowski, 1998).

PNN requires the selection of the optimal value for the width (σ^2) of the radial basis function. For optimizing σ^2 and selecting the relevant input variables, PNN models were trained and evaluated by the bootstrap method, considering each possible combination of scores and varying the values σ^2 in the interval [0.1, 1]. Briefly, bootstrapping generates training sets drawing samples with replacement from the original data set.

For the SVM, the appropriate kernel function, the number of PC scores to be used as input variables and the parameter C were evaluated using the same bootstrap approach applied to the PNN. The input set was determined considering each possible combination of scores. All SVM models were trained over the range C={0.1, 1, 10, 100, 1000} using linear, polynomial and Gaussian kernels (Lai et al., 2009).

Table 1
Subject's characteristics.

	Control group	PD patients
Age (years)	50.1 ± 7.8	56.4 ± 8.3
Mass (kg)	90.56 ± 15.7	50.52 ± 8.02
Height (m)	1.73 ± 0.08	1.67 ± 0.09
Duration of PD (years)	12.2 ± 4.3	N.A.
Time since surgery (months)	15.1 ± 9.5	N.A.