EVALUATION OF THE EFFECTS OF DEEP BRAIN STIMULATION ON GROUND REACTION FORCE IN PARKINSON DISEASE PATIENTS USING PRINCIPAL COMPONENT ANALYSIS

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Abstract
Principal component analysis (PCA) was applied to the vertical component of the ground reaction force (vGRF) for evaluation of the effects of deep brain stimulation of the subthalamic nucleus (STN-DBS) in Parkinson disease (PD) subjects with and without medication. A sample of 10 PD subjects who underwent STN-DBS was evaluated under four test conditions: without any treatment (mof-sof), only with stimulation (mof-son), only with medication (mon-sof), and with both treatments (mon-son). A control group of 30 subjects was also evaluated. PCA was applied on right and left vGRF and the first eight principal components (PC) were retained by broken stick criterion. A standard distance was calculated to measure how far the PD group’s gait was from the normal pattern. The waveform of vGRF improved with treatment, primarily in the mon-son condition. However, there was no statistical difference in the discrete parameters of the first and second peak of vGRF among test conditions. The classification performance had 95% accuracy, 90.0% sensitivity and 96.7% specificity for the cut-off distance 4.18, determined by logistic regression. The smallest ensemble mean value of the standard distance was found in the mon-son condition, which was statistically different from mof-sof. Thus, PCA allowed the quantitative evaluation of the effects of treatments, indicating that STN-DBS improves the vGRF pattern in PD subjects, primarily in combination with PD medication.

Keywords— principal component analysis, ground reaction force, Parkinson disease, deep brain stimulation

Resumo
A análise de componentes principais (ACP) foi aplicada ao componente vertical de força de reação do solo (vFRS) para avaliação dos efeitos da estimulação cerebral profunda do núcleo subtalâmico (ECP-NST) em sujeitos com Síndrome de Parkinson (SP) com e sem medicação. Dez sujeitos com SP submetidos à ECP-NST foram avaliados em quatro situações de teste: sem tratamento (mof-sof), somente com estimulação (mof-son), somente medicamento (mon-sof) e com os dois tratamentos (mon-son). Um grupo controle com 30 sujeitos normais foi também avaliado. A ACP foi aplicada à vFRS do membro direito e esquerdo, e os oito primeiros componentes principais foram retidos pelo teste broken stick. A distância padrão foi calculada para medir a distância da vFRS dos sujeitos com SP ao centróide do grupo normal. A forma da curva da vFRS melhorou com os tratamentos aplicados nos sujeitos com SP, principalmente na condição mon-son. Entretanto, não houve diferença estatística nos parâmetros discretos do primeiro e segundo pico de força da vFRS entre as situações de teste. O desempenho do classificador foi de 95% de acurácia, 90% de sensibilidade e 96.7% de especificidade para uma distância com ponto de corte de 4,18, determinada pela regressão logística. O menor valor médio da distância padrão ocorreu na condição mon-son, o qual foi estatisticamente diferente da mof-sof. Assim, a ACP permitiu a avaliação quantitativa dos efeitos dos tratamentos, indicando que a ECP-NST melhorou o padrão da vFRS dos sujeitos com SP, principalmente associada com a medicação.

Palavras-chave: análise de componentes principais, força de reação do solo, síndrome de Parkinson, estimulação cerebral profunda.
Effect of deep brain stimulation on ground reaction force in Parkinson disease

1. Introduction

Parkinson disease (PD) is a neurodegenerative disorder characterized by bradykinesia, rigidity, tremor and in advanced stages, postural instability. The characteristic slow, short step, shuffling walking pattern results from a combination of constraints on locomotor control imposed by neurotransmitter imbalances (Allert et al., 2001). Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is commonly performed as a treatment of advanced PD. This therapy has been shown to relieve the primary motor symptoms and often allows a significant reduction in dopaminergic medications (Ferrarin et al., 2005). Many studies have demonstrated the effects of DBS, usually by clinical assessment of improvements in motor function (Ferrarin et al., 2005; Davis et al., 2006; Temel et al., 2006). This qualitative approach is inadequate for gait analysis, which is better assessed by quantitative techniques (Krystkowiak et al., 2003). Few studies have evaluated the gait pattern of PD patients, focusing on spatiotemporal and kinematic gait parameters (Faist et al., 2001; Xie et al., 2001; Krystkowiak et al., 2003) or kinetics (Ferrarin et al., 2005).

To accurately evaluate the extent of gait pattern abnormalities in a patient population, or to assess the changes in gait pattern resulting from a specific treatment, natural correlation that exists between gait variables must be taken into account (Schutte et al., 2000). From the statistical point of view, it is important to have a method that spreads the data out and produces clear distinctions between normal and abnormal conditions. In addition, approaches that capture features of entire curve of recorded data instead of a few parameters may further improve the effectiveness of gait analysis. Principal Components Analysis (PCA) is a multivariate method that reduces the dimensionality of data sets containing a large number of interrelated variables, while retaining the original variance as much as possible (Jolliffe, 2002). In gait analysis, this method has been applied to classify normal and pathologic gait (Deluzio and Astephen, 2007) as well as to calculate normalcy indexes to measure how closely the gait pattern of an individual subject approaches normal. Some studies used parametric gait variables (Schutte et al., 2000; Romei et al., 2004) and others analyzed the complete waveform of kinematic gait data (Tingley et al., 2002; Chester et al., 2007). However, none of these studies analyzed the effect of STN DBS on gait.

The present study aims at describing the application of PCA in the vertical component of the ground reaction force for evaluating the effects of STN DBS on PD subjects with and without medication.

2. Materials and Methods

Ten PD subjects (three women and seven men) with ages of 58.1 ± 7.4 (mean ± SD) years participated in the study. All subjects had undergone bilateral STN DBS and were stable when the study was conducted. Averaged time since surgery was 14.1 ± 10.4 months and duration of the disease was 11.9 ± 4.5 years. A control group with 30 subjects (20 women and 10 men), without any neurological or musculoskeletal disorders, with ages of 50.1 ± 7.8 years was also evaluated. Subjects signed an informed consent approved by the Local Ethics Committee.

2.1 Testing procedure

For each PD subject quantitative gait measurement was obtained on two different days. In the first session, the subject had taken his/her usual doses of PD medications and stimulators were turned on. The gait assessment was first conducted with medication and stimulation (mon-son). After the test, the stimulator was turned off for 30 minutes, and the measurements were repeated without stimulation (mon-sof). In the second session, the subjects came to the laboratory without having taken any PD medication for at least 12 hours. Gait analysis was first conducted with stimulation (mof-son), and repeated after 30 minutes without stimulation (mof-sof).

2.2 Gait analysis and signal processing

Two force platforms (AMTI, Watertown, MA) and a three-dimensional motion analysis system (OPTOTRAK, Northern Digital Inc., Waterloo, Ontario) were used in the gait analysis. A total of 12 markers were taped onto the skin of the rear foot, shank, thigh, and pelvis. In this report, only the vertical component of the ground reaction force (vGRF) from the right and left sides and the gait speed were analyzed. All subjects practiced the walking trial on an elevated walkway 12 cm above the floor at least five times before the experiment. Two force platforms were mounted in series and occluded by a carpet at the middle of the walkway. The subjects walked at their self-selected speed and repeated the walking until five successful trials during the evaluation. In each trial, the vGRF and kinematic signals were collected for 10 seconds at a sample frequency of 100 Hz. For each subject, the vGRF was normalized by his/her body weight. The averaged vGRF data from five walking trials was filtered using a low pass Butterworth filter, with a cut-off frequency of 30 Hz. The data were interpolated and re-sampled with 101 points according to the stance phase duration from each lower limb.
2.3 Principal component analysis

The averaged vGRF data from control and PD subjects in the mof-sof condition was organized in a matrix $E$ (40x202), with each row corresponding to data from each subject and each column corresponding to the re-sampled 101 points of right and 101 of left limb from vGRF for one subject. Principal component analysis (PCA) was applied to the covariance matrix derived from $E$, to calculate the corresponding covariance matrix $S$ (202 x 202), with elements $s_{jk}$ given by (Jolliffe, 2002):

$$s_{jk} = \frac{1}{N-1} \sum_{i=1}^{N} (e_{ij} - \bar{e}_j)(e_{ik} - \bar{e}_k)$$  \hspace{1cm} [1]

where $N = 40$, $\bar{e}_j$ and $\bar{e}_k$ are the values of the ensemble mean of the corresponding samples $j$ and $k$.

The principal components (PCs) were obtained by the solutions of the linear system given by:

$$S\cdot x_p = \lambda_p\cdot x_p$$  \hspace{1cm} [2]

where $\lambda$ are the eigenvalues of $S$ ranked in decreasing order and $x$ are the corresponding normalized eigenvectors (PCs). Each PC is thus an independent waveform feature based on the variability in the original waveform data set. The first PC corresponds to the largest source of variation; the second PC corresponds to the second largest source of variation, orthogonal to the first, and so on. A broken stick test criterion was used in selecting the relevant PCs for the analysis (Jackson, 1993). The matrix of PC scores ($Z$) of the control subjects and PD subjects in the mof-sof condition were calculated by the product (Jolliffe, 2002):

$$Z = X\cdot E$$  \hspace{1cm} [3]

2.4 Normalcy index

To obtain a measure of how far the PD subjects’ gait was from that of the control group, the standard distance proposed by Flury and Riedwyl (1986) was calculated from the scores of the selected PCs. This parameter represents the distance between each observation and the center of the ellipsis in the plane of the PC scores, normalized by the variance of each score.

For classifying normal or abnormal vGRF pattern, the cut-off point between standard distance values from the control group and PD group in the mof-sof condition was obtained by logistic regression (Muniz and Nadal, 2009). The classifier performance was assessed by the leave-one-out cross-validation technique, which provides a good indication of reliability in classification of small datasets. Of 40 observations (30 normal and 10 PD subjects in the mof-sof condition) one was removed and further compared with the cut-off point given by the remaining 39. Afterwards, the data point was replaced in the dataset and another observation was removed to repeat the procedure. This process was repeated until each observation had been left out in turn. The results of each comparison were used to assess the performance of the classifier, by computing overall accuracy, sensitivity (correct classification of PD) and specificity (correct classification of controls).

2.5 Effects of treatments

The PC scores from PD subjects in the treatment conditions mon-sof, mof-sof, and mon-sof were obtained by the scalar product between each PC and the vGRF from each condition. To assess the effect of each treatment condition, values of the standard distance obtained from PD subjects in four testing conditions were compared. The standard distances in three treatment conditions were also applied to the above-described classifier for determining the vGRFs that reached the normalcy boundary.

The gait velocity and the first and second peak of vGRF were also measured for PD subjects in the four testing conditions.

2.6 Statistical analysis

Non-parametric Friedman test for repeated measures was applied to verify differences among treatments in the standard distance, gait velocity and the first and second peaks of force. Post hoc analysis was then performed with the Dunn test. The Wilcoxon Rank Sum test was applied to compare differences between PC scores from control and PD subjects in the mof-sof condition. The significance level was set to $p = 0.05$. All signal processing procedures and statistical tests were implemented in Matlab 6.5 (The Mathworks, USA).

3. Results

The waveform of vGRF improved with the PD treatments, primarily in the mon-sof condition (Figure 1). However, there was no statistical difference in the discrete parameters of the first and second peak of vGRF among test conditions. Only in the mon-sof condition did gait velocity show a significant increase from mof-sof condition (Table 1).

Table 1 – Discrete gait variables for PD subjects in the four different conditions.

<table>
<thead>
<tr>
<th>Condition</th>
<th>1st vGRF peak (% BW)</th>
<th>2nd vGRF peak (% BW)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mof-sof</td>
<td>1.03 ± 0.06</td>
<td>0.99 ± 0.07</td>
</tr>
<tr>
<td>mon-sof</td>
<td>1.06 ± 0.07</td>
<td>1.00 ± 0.05</td>
</tr>
<tr>
<td>mof-sof</td>
<td>1.06 ± 0.05</td>
<td>1.01 ± 0.03</td>
</tr>
<tr>
<td>mon-sof</td>
<td>1.07 ± 0.05</td>
<td>1.03 ± 0.03</td>
</tr>
</tbody>
</table>
The broken stick test indicated that eight PCs should be used in the analysis, which explained 94.36% of the total variance of the original data.

The standard distance allowed the classification of vGRF pattern with 95% accuracy, 90% sensitivity and 96.7% specificity, with a cut-off point of 4.18. In the mof-sof condition, one subject was classified as normal, while this number increased to five for mof-son, and to six for mon-son, indicating the mon-son condition was the closest to control group as shown in vGRF curve (Table 2 and Figure 1). A significant difference among conditions (p = 0.0293) was observed, with the post hoc test recognizing a difference only between the mof-sof and mon-son conditions.

4. Discussion

The shape of the vGRF showed qualitative changes in all treatment conditions (Figure 1).
However, the first and second peaks of vGRF, commonly analyzed in previous studies (Hsiang and Chang, 2002; Li and Hamill, 2002) did not indicate differences among test conditions. Such parametric analysis did not consider the high degree of correlation among various aspects of subjects’ gait (Tingley et al., 2002; Ferrarin et al., 2005). The gait speed, however, increased in the mon-son condition compared with the mo-sof condition, as observed in other studies (Faist et al., 2001; Ferrarin et al., 2005). This provides a picture of gait quality, but not enough information about its pattern, since it did not take into account atypical gait waveforms pattern (Schwartz and Rozumalski, 2008).

The standard distance allowed quantification of changes in vGRF shapes and recognition of how far PD subjects’ gait pattern was from normality. Such an index has been used to evaluate specific treatments (Tingley et al., 2002; Romei et al., 2004), as well as to identify gait pattern (Chester et al., 2007; Schwartz and Rozumalski, 2008). With STN-DBS, the standard distance reduced with stimulation and medication (mon-son), evidencing improvement in gait pattern. Past studies have also reported enhancements in gait performance with stimulation (Faist et al., 2001; Ferrarin et al., 2005) and further improvement when combined with medication (Krystkowiak et al., 2003; Ferrarin et al., 2005).

These results suggest a greater effect on vGRF patterns with stimulation alone compared to medication alone (Table 2). Faist et al. (2001) reported almost identical mean values in gait parameters between a supra-threshold dose of medication and stimulation. Krystkowiak et al. (2003) found better results with medication. A possible explanation for this disagreement is differences in the experimental protocols. In the present study the medication condition refers to the usual dose of medicine rather than a “super-threshold” levodopa dose to better represent the daily living condition of patients (Liu et al., 2005).

5. Conclusion

The use of principal component analysis, standard distance and logistic regression allowed delimiting a normalcy point that quantitatively evaluated the gait improvements in PD due to different treatments. DBS of the STN showed effective improvement on vertical ground reaction force, with the pattern being nearly normal in PD subjects when STN stimulation was combined with PD medication.

References


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