Analysis of the Severity of Dyskinesia in Patients with Parkinson's Disease via Wearable Sensors

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Abstract

The aim of this study is to identify movement characteristics associated with motor fluctuations in patients with Parkinson's disease by relying on wearable sensors. Improved methods of assessing longitudinal changes in Parkinson's disease would enable optimization of treatment and maximization of patient function. We used eight accelerometers on the upper and lower limbs to monitor patients while they performed a set of standardized motor tasks. A video of the subjects was used by an expert to assign clinical scores. We focused on a motor complication referred to as dyskinesia, which is observed in association with medication intake. The sensor data were processed to extract a feature set responsive to the motor fluctuations. To assess the ability of accelerometers to capture the motor fluctuation patterns, the feature space was visualized using PCA and Sammon's mapping. Clustering analysis revealed the existence of intermediate clusters that were observed when changes occurred in the severity of dyskinesia. We present quantitative evidence that these intermediate clusters are the result of the high sensitivity of the proposed technique to changes in the severity of dyskinesia observed during motor fluctuation cycles.

Keywords: Wearable Sensors, Clustering, Parkinson's Disease, Dyskinesia

1. Introduction

Parkinson's disease (PD) is the most common disorder of movement, affecting about 3% of the population over the age of 65 years and more than 500,000 US residents. The characteristic motor features are development of rest tremor, bradykinesia, rigidity, and impairment of postural balance. The primary biochemical abnormality in PD is deficiency of dopamine due to degeneration of neurons in the substantia nigra pars compacta [1]. Current therapy of PD is based primarily on augmentation or replacement of dopamine, using the biosynthetic precursor levodopa or other drugs, which activate dopamine receptors. These therapies are often successful for some time, but most patients eventually develop motor complications [2][3]. Complications include *wearing off*, the abrupt loss of efficacy at the end of each dosing interval, and *dyskinesias*, involuntary and sometimes violent writhing movements [5][6]. Currently available tools for managing motor fluctuations are quite limited. In clinical practice, information about motor fluctuations is usually obtained by asking the patient to recall the number of hours of ON and OFF time they have experienced in the recent past. "ON time" is used to refer to periods when medications are effective in attenuating symptoms. "OFF time" is used to refer to periods when symptoms are present. This kind of self-report is subject to both perceptual bias and recall bias. A reliable quantitative tool for evaluating motor complications in PD patients would be valuable both for routine clinical care of patients as well as for trials of novel therapies. In the study, we explored the use of

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miniature, wearable sensors to capture movement features that are associated with changes in the severity of dyskinesia as they occur during the intervals between medication intakes.

2. Methods

2.1 Data Collection

Twelve individuals were recruited in the study, ranging in age from 46 to 75 years, with a diagnosis of idiopathic Parkinson's disease (Hoehn & Yahr stage 2.5 to 3, i.e. mild to moderate bilateral disease with ability to recover from sudden postural disturbance or with some postural instability). Subjects were assessed on the day of the experiment by a clinician using the Unified Parkinson's Disease Rating Scale (UPDRS) [4].

Figure 1 schematically represents the motor fluctuation cycle. Subjects were asked to delay their first medication intake in the morning so that they could be tested in a "practically-defined OFF" state. This approach is clinically used to observe patients in the period of most severe parkinsonian symptoms. Subsequently, patients took their medications and were tested at 30-minute intervals thereafter until the following medication intake, in order to gather sensor data during an entire motor fluctuation cycle.

Accelerometer sensors were used to gather biomechanical signals during standardized motor tasks utilized for clinical assessment including sitting, finger-to-nose movements, finger tapping, alternating hand movements, leg agility, sit-to-stand, walking, and stand-to-sit. For each task, 30 s of sensor data were recorded. Accelerometers were placed on the right and left upper arm, right and left forearm, right and left thigh, right shin, and left shin. The sensors were connected to an ambulatory system (Vitaport 3, Temec BV, The Netherlands) equipped with data acquisition hardware and software to collect and store the signals. Subjects were videotaped throughout the experiment, and motor UPDRS and dyskinesia scores were assigned for each task by review of the videotapes.

Figure 1 Schematic representation of a motor fluctuation cycle. See text for details.

2.2 Feature Extraction

Sets of ten 5-second epochs were randomly selected from the 30 s of sensor data corresponding to each task, for each testing interval. To facilitate visualization of the data, it was necessary to reduce the dimensionality of each dataset by selecting features that captured the characteristic accelerometer patterns associated with motor fluctuations. Before extracting features, the raw data were high-pass filtered with a cutoff frequency of 1 Hz to remove the gross orientation changes and low-pass filtered with a cutoff frequency of 15 Hz to remove the high frequency noise. The features were chosen to represent characteristics such as intensity, modulation, rate, periodicity, and coordination of movement. Intensity was measured as the root-mean-square (RMS) value of the detrended accelerometer signal. The modulation of the output of each sensor was used to represent dynamic characteristics of the tasks, and was calculated as the range of the auto-covariance of each channel. Large values of this feature were indicative of intervals of rapid movements interspersed with intervals of slow movements. Rate of movement was represented by the dominant frequency component below 10 Hz. Periodicity was measured by computing the ratio of energy in the dominant frequency component to the total energy below 10 Hz. Coordination between body segments on the left and right side and proximal and distal segment was captured in three aspects: magnitude (obtained by calculating the correlation coefficient), delay (estimated as the time lag corresponding to the peak of the cross-correlation function) and similarity (measured by the value of the peak of the cross-correlation function).

To study dyskinetic movements, features were derived from the lower extremity accelerometer channels during a task requiring fine motor control of the upper extremities (e.g. finger tapping). This was done because dyskinesias are more likely to be observed (i.e. less prone to suppression) in the lower extremities when the patient's attention is focused on a fine motor control task involving the upper extremities.

2.3 Feature set visualization

Further processing was necessary in order to visualize the features sets and assess whether data from the sensors were meaningfully related to clinical scores and/or the time course of the experiment. Suitable approaches to projecting high-dimensional data sets into a low-dimensional space include principal components analysis (PCA) [9] and Sammon's mapping [10]. Both approaches were incorporated in the analysis. In order to reduce computational

complexity and minimize the influence of redundant features, a PCA was first applied to the normalized feature set, and the first 6 PCs (accounting for more than 90% of the total variance) were retained. Then, the Sammon's map method was applied to the PCA-transformed features to obtain a two-dimensional representation of the data.

2.4 Clustering

Clustering of the feature space was then performed. Visualization using Sammon's mapping showed evidence of clusters, which were labeled by the clinical scores. We applied the expectation maximization (EM) algorithm to find natural clusters in the feature space and used those clusters as labels for the visualization. EM is a statistical model that makes use of the finite Gaussian mixtures model [11]. The algorithm is similar to the K-means procedure in that sets of parameters are re-computed until a desired convergence value is achieved. This gave us a useful insight into the characteristics of the sensor data as reflected in the feature space. To quantitatively analyze the clustering process, we used the Dunn's index for cluster validity [12]. A large value for Dunn's indices indicates that the clusters are compact and well separated. Finally, the Euclidian distance among pairs of clusters was computed in the feature space to explore the relationship between clusters and associated clinical scores. This was useful to investigate the possibility that some clusters may represent intermediate scores among those assigned by clinicians thus suggesting high sensitivity of the proposed method to changes in dyskinesia.

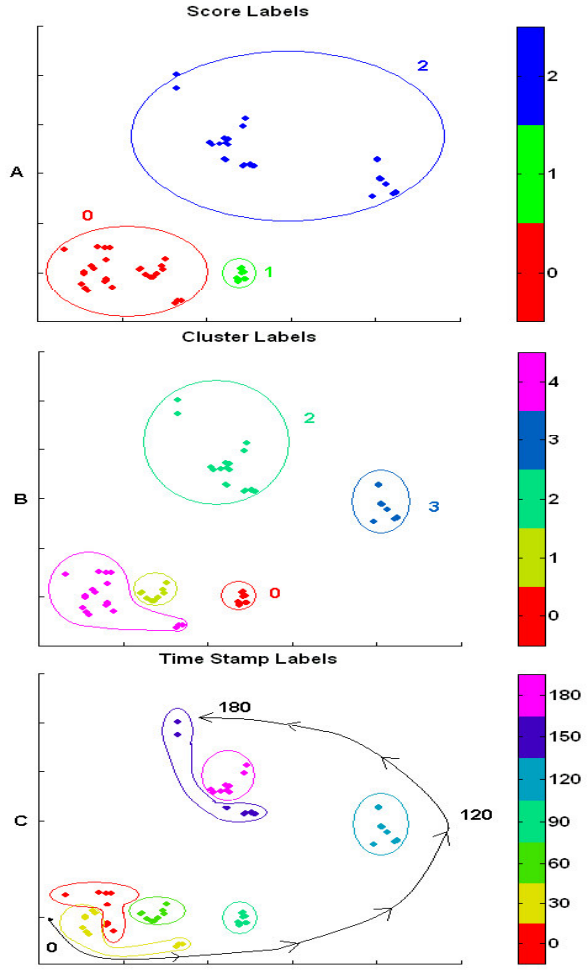

Figure 2 Sammons maps labeled by (A) scores, (B) EM clusters and (C) time stamps.

3. Results

Of the 12 subjects tested, 5 showed significant modulation of dyskinesia scores. Figure 2 shows 3 Sammons maps of the same feature set but labeled in three different ways. The feature set was extracted from data that were collected during the left hand finger to nose task. In the first plot (Figure 2(A)), data are labeled by clinical scores provided by an expert neurologist via visual inspection of the patients during the tests. The second plot (Figure 2(B)) has labeled derived from clustering of the feature set via the EM algorithm. In the third plot (Figure 2(C)), data are labeled by time stamps i.e. the time at which the data were collected. Observing the plots, it is evident that clusters closely followed the different times at which data were collected. This is an indication that we could be able to predict, from the sensor data, intermediate states, which would give us the ability to closely monitor patients. Figure 2(C) shows the correspondence between clusters and time of the experiments from 0 to 180 min. Figure 3 shows the dyskinesia scores at different time intervals. We see that the score is zero during the pretest (i.e. time 0) and

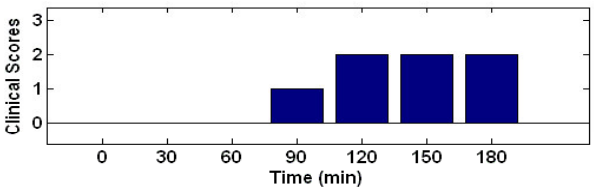

Figure 3 Changes in dyskinesia clinical score over time for the subject whose data are shown in Figure 2.

increases during subsequent tests to a score of 2. There is a correspondence between these results and the results of the analyses shown in Figure 2.

Visual inspection of the clusters in the 2D space shows good separation of the datasets. Quantitative analysis via Dunn's indices confirmed that the clusters are well separated and showed that closer clusters have the same clinical score. Table 1 shows the Dunn's indices for all the pairs of clusters identified via the EM algorithm calculated in the 15 dimensional feature space. Dunn's indices are relatively large for most of the cluster pairs, which indicates that the clusters are well separated and tight. Table 2 shows the distances between cluster centers (also calculated in the 15 dimensional feature space). Note that in Figure 2(B) cluster 3 corresponds to a dataset that was assigned a clinical score of 2 as shown in Figure 2(A). Looking at the cluster center distances in Table 2, it appears that cluster 3 is indeed closer to cluster 2 than cluster 0 is to cluster 3 (Figure 2(B)).

Table 1. Dunn's Indices

Cluster	0	1	2	3	4
0	*0*	*4.70*	*3.62*	***8.55***	*2.68*
1		*0*	*4.20*	*7.20*	***1.37***
2			*0*	*2.82*	*3.04*
3				*0*	*4.57*
4					*0*

Table 2. Cluster Center Distances

Cluster	0	1	2	3	4
0	*0*	*6.53*	*5.23*	***5.05***	*7.56*
1		*0*	*9.48*	*9.60*	*2.06*
2			*0*	***1.02***	*10.27*
3				*0*	*10.33*
4					*0*

4. Conclusion

We demonstrated that accelerometer data allow one to capture changes in dyskinesia that occur in patients with PD during motor fluctuation cycles. The results of our qualitative and quantitative analysis show that the feature sets that we extract from accelerometer data can be used to build reliable predictors of clinical scores. An interesting observation was the existence of intermediate stages that could potentially provide useful qualitative information about the motor fluctuations of patients with PD. Future studies will expand the analysis to other motor complications in patients with PD. Our preliminary results suggest the usefulness of a wireless wearable sensor system that could be used to facilitate medication titration via monitoring in the home environment.

Acknowledgments

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References

[1] DG Standaert, AB Young, in Goodman and Gilman's Pharmacological Basis of Therapeutics, Tenth Edition, Hardman JG and Limbird LE, Editors, McGraw-Hill, 549-620, 2001.

[2] TN Chase, "Levodopa therapy: consequences of the non physiologic replacement of dopamine", Neurology, 50(Suppl5): S17-S25, 1998.

[3] JA Obeso, CW Olanow, JG Nutt, "Levodopa motor complications in Parkinson's disease", Trends Neurosci, 23: 2-7, 2000.

[4] S Fahn, RL Elton, "Unified Parkinson's Disease Rating Scale". In Fahn S (Ed), Recent Developments in Parkinson's Disease, MacMillan Healthcare Information, 153-163, 1987.

[5] AE Lang, AM Lozano, "Parkinson's disease. First of two parts", N Engl J Med, 339(16): 1044-1053, 1998.

[6] AE Lang, AM Lozano, "Parkinson's disease. Second of two parts", N Engl J Med, 339(16): 1130-1143, 1998.

[7] PJ Blanchet, SM Papa, LV Metman, MM Mouradian, TN Chase, "Modulation of levodopa-induced motor response complications by NMDA antagonists in Parkinson's disease", Neurosci Biobehav Rev, 21: 447-453, 1997.

[8] MM Mouradian, IJ Heuser, F Baronti, TN Chase, "Modification of central dopaminergic mechanisms by continuous levodopa therapy for advanced Parkinson's disease", Ann Neurol, 27(1): 18-23, 1990.

[9] IT Jolliffe, Principal Components Analysis. New York: Springer-Verlag, 1986.

[10] MP Sammon, EN Bruce, "Vagal afferent activity increases dynamical dimension of respiration in rats", J Appl Physiol, 70(4): 1748-1762, 1991.

[11] RO Duda, PE Hart, DG Stroke, "Pattern Classification", 2nd edition, Wiley Interscience, 2001.

[12] JC Bezdek, NR Pal "Some new indexes of cluster validity", IEEE Transactions on System, Man, and Cybernetics-part B: Cybernetics, Vol. 28, No. 3, June 1998.