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Dyskinesia and motor state detection in Parkinson's Disease patients with a single movement sensor*

A. Samà, C. Pérez-Lopez, J. Romagosa, D. Rodríguez-Martín, A. Català, J. Cabestany, D.A. Pérez-Martínez and A. Rodríguez-Molinero

Abstract— **Parkinson's Disease (PD) is a neurodegenerative disease that alters the patients' motor performance. Patients suffer many motor symptoms: bradykinesia, dyskinesia and freezing of gait, among others. Furthermore, patients alternate between periods in which they are able to move smoothly for some hours (ON state), and periods with motor complications (OFF state). An accurate report of PD motor states and symptoms will enable doctors to personalize medication intake and, therefore, improve response to treatment. Additionally, real-time reporting could allow an automatic management of PD by means of an automatic control of drug-administration pump doses. Such a system must be able to provide accurate information without disturbing the patients' daily life activities. This paper presents the results of the MoMoPa study classifying motor states and dyskinesia from 20 PD patients by using a belt-worn single tri-axial accelerometer. The algorithms obtained will be validated in a further study with 15 PD patients and will be enhanced in the REMPARK project.**

I. Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease after Alzheimer's disease. It is a progressive neurological condition resulting from the degeneration of dopamine producing neurons in the *substantia nigra*, which is located within midbrain or mesecephalon. Though PD can manifest itself at any age, it is unusual in persons under 30 years and only 10% of cases start before 40. According to the World Health Organization, 5.2 million people suffer PD in the World and mortality is two to five times higher among affected persons than among age-matched controls.

PD symptoms are caused by a decrease in the levels of dopamine, due to the death of the nerve cells in the brain that produce it. Levodopa (or similar medication) increases dopamine production. The main problem when PD patients take levodopa or similar drugs is the fluctuation between "almost normal" periods from the motor symptoms point of view, known as ON periods, and periods where motor symptoms are more evident, known as OFF periods. Although disease experience is variable, patients in a moderate or severe stage of the disease will cycle between ON and OFF periods from three to four times every day. With the help of their neurologists, patients need to learn to schedule their medication and their activities around their ON/OFF cycles. During ON periods, patients report that they feel relatively clear and in control of their movements. Often during these times, symptoms of PD may be imperceptible to all but professionals, except for dyskinesia (involuntary movements). During OFF periods, Parkinson's symptoms either re-emerge or worsen before the next dose of medication. Patients can experience the full range of classic PD symptoms: tremor, stiffness, bradykinesia (slowness of movement), postural alteration, lack of muscular coordination, difficult handwriting and they also experience more frequently the symptom called freezing of gait (FOG).

An accurate reporting of PD motor states and symptoms will enable doctors to personalize medication intakes and, therefore, improve the response to treatment. Moreover, real-time reporting could allow an automatic management of PD by means of a drug-administration pump regulated by a Personal Health System (PHS). Such a system should be able to provide accurate information without disturbing the patient's daily life activities. MicroElectroMechanical Systems (MEMS), mainly accelerometers and gyroscopes, have been widely used to analyze PD movement. A remarkable recent study was presented in 2010 by Zwartjes et al. [1], in which motor activities (sitting, walking, etc.) and severity related to tremor, bradykinesia and hypokinesia were analyzed. Six PD patients each wore four sensors at wrist (for tremor detection when resting), thigh (for standing/ sitting detection), foot (walking) and sternum (lying/standing posture). Results showed that the method's output is correlated with Unified Parkinson's Disease Rating Scale (UPDRS) values. Another important study was presented by Salarian et al. [2]. They detected and quantified tremor and bradykinesia in 20 PD patients by using two tri-axial gyroscopes located on each of the forearms. Results showed a high correlation with related UPDRS values.

In order to increase usability it is important to detect PD symptoms with a minimum number of devices. This work presents a study detecting ON and OFF motor states and dyskinesia by using a single accelerometer worn on a belt in a population of 20 PD patients. The study is part of the Monitoring the Mobility of PD Patients for Therapeutic Purposes (MoMoPa) project, and the resulting methods are

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A. Samà, C. Pérez-Lopez, J. Romagosa, D. Rodríguez-Martín, A. Català and J. Cabestany are with the Technical Research Centre for Dependency Care and Autonomous Living (CETpD), Technical University of Catalonia (UPC), Vilanova i la Geltrú 08800 Spain (e-mail: albert.sama@upc.edu, carlos.perez-lopez@upc.edu, jaume.romagosa@upc.edu, daniel.rodriguez-martin@upc.edu, andreu.catala@upc.edu, joan.cabestany@upc.edu).

D.A. Pérez-Martínez is with the University Hospital Infanta Cristina, Parla (Madrid) 28981 Spain (e-mail: daperezm@salud.madrid.org).

A. Rodríguez-Molinero is with Centro Médico Artis, Sant Pere de Ribes, 08810 Spain, also with Consorci Sanitari Garraf, Vilanova i la Geltrú, 08800 Spain, and NUI Galway, Galway, Ireland (e-mail: arodriguez@centromedicoartis.com).

being tested in another experiment, which is also part of MoMoPa project, performed under real-life conditions for several hours with 15 PD patients. The results obtained in this last stage will be employed as part of the background exploited in the Personal Health Device for the Remote and Autonomous Management of PD (REMPARK) project. REMPARK aims to develop a PHS for the improved management of PD. Finally, an enhanced version of the algorithms presented in this paper will be used in the Home-based Empowered Living for PD Patients (HELP) project, which will test the use of an apomorphine infusion pump regulated according to previously established clinical rules based on symptom's information provided by sensors [13].

II. Materials and Methods

A. Participants and data acquisition

The study was divided into two phases and a total of 20 PD patients participated in it. Patients who participated had an idiopatic Parkinson according to UK PD Society Brain Bank criteria [12] with ages from 49 to 82 years and were in a mild or moderate stage of the disease. For security reasons, patients with implanted electronic devices were excluded.

Patients performed various activities while an inertial sensor located at their waist registered acceleration, angular velocity and magnetic field measurements. In this study only accelerations are used, the other measurements will be employed in further analysis. More specifically, ten patients performed the first phase protocol which consisted of walking three times in a straight line of ~five m. in laboratory. Patients also wore movement sensors in both shanks, which enabled the validation of the stride-detection algorithm presented in subsection *C*. Ten other patients performed the second phase protocol, which included activities in the laboratory and outdoors. Laboratory activities comprised walking in a straight line, walking over an inclined plane, carrying a heavy object, setting a table and going upstairs and downstairs. The outside protocol consisted of walking for, at least, 15 minutes. Patients that had motor fluctuations repeated the experiment in OFF state, induced by avoiding the first morning intake of medication. The experimental protocol was approved by the local Ethics Review Committee. Participants had a mean (st. deviation) age of 64.4 (9.3).

A device developed at CETpD was used to register the measures during experiments. The device included various MEMS sensors: a tri-axial LIS3LV02DQ accelerometer (±6g range), Invensense IDG650 + ISZ650 gyroscopes (±2000º/s range) and Honeywell HMC6042 + HMC1041Z magneto-meters (±1.5 Gauss range). Only acceleration measures were used according to the methods presented in this paper. The device also included a dsPIC33F microcontroller and a Li-ion battery of 1130mAh. The sampling frequency was 200 Hz. All signals were filtered by using a 2nd order low-pass Butterworth filter with 15 Hz cut-off frequency. Activities performed in laboratories were videotaped by 2 cameras. During the outdoor protocol, activities and symptoms were labeled by a trained observer who used an annotation software running on a PDA.

B. Dyskinesia detection

Dyskinesia symptoms consist of involuntary movements which are associated with chronic levodopa therapy in PD. Dyskinesia most commonly occurs when antiparkinsonian effects of levodopa are maximal, i.e. during ON states, or when the patient is switching between ON and OFF phases (biphasic dyskinesia). Thus, a dyskinesia detector is helpful to identify the motor state of a patient.

The dyskinesia detection approach used in this work is based on a review of literature. It has been previously observed that dyskinesia increases the power spectrum of the accelerometer frequency band between 1-4 Hz. Manson et al. demonstrated it for an accelerometer located at patient's shoulder [3], and Keijsers et al. also showed it for 6 accelerometers located at upper arms, upper legs, wrist and trunk [4]. It is important to note that walking activity makes harmonics appear in the full spectrum. For that reason, the activity was removed from the analysis of the former study in order to avoid false positives on dyskinesia detection.

The dyskinesia detection method used in this study consists of analyzing the spectrum of the waist accelerometer signals obtained. It was considered that whenever the power spectrum between 1 and 4 Hz exceeded a certain threshold th_1, the patient was suffering dyskinesia. Additionally, the power spectrum until 20 Hz must be under another threshold th_2 in order to avoid the false positives. This way, false positives that could occur during gait, or other similar activities that fill the whole power spectra like ascending or descending stairs, are avoided.

Every 1.6 sec. the algorithm evaluates the frequency content of the last 3.2 s. provided by each accelerometer's axis. Accordingly, a positive detection occurs when the sum of the power spectra between 1 and 4 Hz exceeds th_1 and the sum of the power spectra until 20 Hz does not exceed th_2. This condition must be held during various consecutive analyses, i.e. during at least w seconds. This window length adds some robustness to the method and was set to 6 seconds, according to the minimum duration of the activities.

C. ON and OFF motor states detection

During OFF states, various movement disorders that alter the patient's gait appear: rigidity, bradykinesia, freezing of gait, festination and postural instability. During ON states, symptoms are alleviated and patients move more smoothly. In this study, ON and OFF motor states detection was focused on gait analysis. The main goal consisted of obtaining a measuring instrument correlated to ON and OFF motor states by means of a single accelerometer located at waist.

The ON and OFF motor states analysis is based on characterizing gait cycles, i.e. strides. A prerequisite is that patient should be walking; thus, a gait detector should enable gait cycles analysis. The latter analysis should perform, on the one hand, an identification of gait cycles from the accelerometer signal, i.e. stride detection, and, on the other hand, should characterize gait cycles by some features that correlates motor states. Then, a three-step ON and OFF characterization method is obtained, which is represented in Fig. 1.

Figure 1. Three-step ON and OFF motor state characterization

Gait detection consists of a pattern recognition process applied to the accelerometer signal in order to identify whether the patient is walking. A bi-class problem arises, hence a Support Vector Machine (SVM) [5] is employed. Its input consists of various features which characterize a 3.2 seconds window of the accelerometer signal. A training dataset was created from phase-one patient data. It consists of more than 800 features obtained from each axis of the accelerometer and their magnitude. This includes min, max, range, median, average, standard deviation; and spectrum power and maximum amplitude in the spectrum or spectra band between $[b_1, b_2]$ Hz s.t. $b_1 > b_2$, b_1 and $b_2 \in [0, 20]$ Hz. The two most significant features in gait detection, i.e. those that maximize inter-class distance and minimize intra-class distance, were selected according to a Relief algorithm [6]. The SVM was trained with data from phase-one patients and validated against data from phase-two patients.

The stride detection process, which is performed when the SVM gives a positive output, takes advantage of how acceleration signals from the lower part of the trunk behave due to biomechanical characteristics of gait, as described in the literature. The onset of gait stance phase, when the heel makes contact with the ground, can be determined by a local minimum in the forward acceleration observed from the lower trunk [7]. This event of the gait cycle is also known as 'Initial Foot Contact' and is considered to establish the starting of a step. However, we are interested in strides, which are composed of two consecutive steps. Discrimination between right and left steps can be performed by analyzing relative extrema on lateral acceleration of the lower trunk, since it approximately describes a sinus period during a gait cycle [8]. Consequently, forward acceleration provides step identification and lateral acceleration allows the determination of strides. Figure 2 shows the result of the stride detection algorithm based on step detection, which was previously used in [9, 10], in a phase-one patient. It also shows the stride detection validation against the gyroscope signal obtained from the shanks. This previously has been shown to determine swing phase [11], during which the foot is off the ground and which is preceded by stance phase as a minimum peak of the signal.

The stride characterization process aims to extract some characteristic from previously detected strides representing the smoothness of movement of the patient, i.e. bradykinesia and rigidity. This way, several statistics are applied and evaluated. The best statistic is considered to be one that maximizes the separation between ON and OFF motor states. Furthermore, we are interested in a representation that linearly separates both motor states and that intuitively represents the smoothness of the movement. Thus, the best statistic should maximize the Area Under ROC Curve (AUC). Furthermore, it is considered that motor states are user-dependent; ideally, the *border* between ON and OFF depends on the stage of the disease and the patient. Thus, the threshold that best distinguishes both motor states in a certain patient is expected to have a different value than the best threshold for another patient. This way, AUC is evaluated separately in each patient.

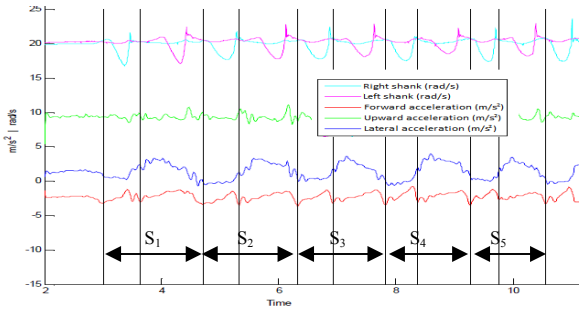

Figure 2. Five strides detected by using a single accelerometer located at waist and the algorithm described. Strides are divided into two steps. Gyroscope signals from shanks that validate the detection are alse shown.

III. Results and Discussion

A. Dyskinesia detection results

Threshold values used for th_1 and th_2 are 1.5 and 1, respectively, which were fixed experimentally by evaluating data from all phase-one patients and from tenth of the phase-two patient (Learning group). The results obtained applying the method to the rest of phase-two patients (Test group) are showed in Table I.

TABLE I. Dyskinesia Results

Patient	Spec.	Sens.	Positive pred. value	Negative pred. value
P_1	0.66	1.00	1.00	0.66
P_2	0.33	1.00	1.00	0.50
P_3	1.00	1.00	1.00	1.00
P_4	0.00	1.00	1.00	0.60
P_5	1.00	1.00	1.00	1.00
P_6	1.00	1.00	1.00	1.00
P_7	1.00	0.00	0.80	1.00
P_8	1.00	1.00	1.00	1.00
P_9	1.00	1.00	1.00	1.00
Average	0.78	0.89	0.98	0.87

The positive predictive value is especially high, which means that when the detector provides a positive result it is highly likely to be true dyskinesia. Although the specificity is not that high, the method provides a good sensitivity. This way, it can be used in real environments to assess ON states.

B. ON and OFF motor states results

The features selected by Relief algorithm as the most relevant for gait detection are the tri-axial power spectra between [0.1, 3] Hz and [0.1, 10] Hz. The training set, obtained from phase-one patients' data, was used to train a SVM by a 10-fold CV with a RBF kernel. The validation of SVM on the testing set obtained from phase-two patient's data provides the following results: specificity 0.84; sensibility 0.90, and accuracy 0.94. These results validate the resulting SVM as a gait detector for PD patients.

The stride characterization process evaluates how several features representing the strides separate ON and OFF motor

states by measuring the AUC. Features maximizing the distance between motor states are expected to represent the smoothness of movement. Tested features are the same as used for gait detection listed in the previous section. Six PD patients had ON-OFF fluctuations, and the results of the best 5 features are shown in table II. The best five features relates to tri-axial power spectra values, more specifically features F_1 to F_5 are power spectra in bands [0, 10], [0, 8], [0, 7], [0, 6] and [0, 5] Hz. How the feature values averaged between 5 consecutive strides affect the results was also tested, in order to add some robustness to the method. The obtained AUC values are shown in Table III.

Results show that an excellent AUC value is provided by the tri-axial power spectra in the band of [0, 10] Hz averaged between 5 strides and used as a linear classifier. This result can be explained according to PD symptoms. The reduction of the step frequency and the shortening of stride length and speed are common PD gait alterations. Fig. 3 shows two typical strides obtained during ON and OFF states and it can be observed that OFF motor state provides less amplitude in both temporal and frequency domains.

It is important to note that data from ON and OFF motor states are quite *pure* in the sense that patients performed the experiments in OFF state by avoiding the first medication intake in the morning. After some recover time, which may took up to 3 hours, the experiments in ON were performed. Hence, the excellent separation between motor states had been facilitated by the bi-modal distribution obtained.

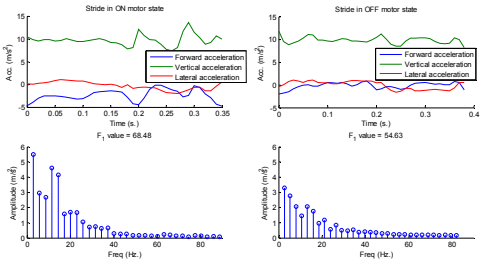

Figure 3. Frequency content of strides in both motor states.

TABLE II. ON-OFF MOTOR STATES RESULTS

Patient	AUC F_1	AUC F_2	AUC F_3	AUC F_4	AUC F_5
P_1	0.820	0.875	0.851	0.812	0.812
P_2	0.904	0.895	0.889	0.858	0.848
P_3	0.822	0.770	0.808	0.767	0.802
P_4	0.855	0.825	0.815	0.883	0.848
P_5	0.889	0.922	0.879	0.898	0.858
P_6	0.805	0.804	0.816	0.781	0.828
Avg.	**0.849**	**0.848**	**0.843**	**0.833**	**0.833**

TABLE III. ON-OFF MOTOR STATES AVERAGING 5 STRIDES

Patient	AUC F_1	AUC F_2	AUC F_3	AUC F_4	AUC F_5
P_1	0.979	0.974	0.981	0.981	0.980
P_2	0.934	0.905	0.894	0.861	0.856
P_3	0.827	0.811	0.816	0.818	0.816
P_4	0.997	0.977	0.960	0.940	0.920
P_5	0.936	0.936	0.921	0.905	0.890
P_6	0.997	0.997	0.997	0.997	0.997
Avg.	**0.945**	**0.933**	**0.928**	**0.917**	**0.910**

The last stage of this study is testing the algorithms obtained in a continuous monitoring of fifteen PD patients during approximately six hours in their own home. The experiments have already been performed and data obtained are being analyzed by means of the presented methods.

IV. CONCLUSIONS

This work presents a method to detect dyskinesia and to characterize motor states in PD patients. The dyskinesia method has been applied to nine PD patients and the ON-OFF method to six patients who showed motor states fluctuations. According to the results, a single belt-worn accelerometer is enough to accurately differentiate *pure* ON and OFF states and to detect dyskinesia with a high positive predictive value.

The method for dyskinesia detection showed in this paper is based on other works [3, 4]. The statistical analysis of strides presented is, to the best knowledge of the authors, a novel method which provides a new insight in the gait frequency content in PD.

The methods presented in this work are being applied to a new continuous monitoring experiment with 15 PD patients under real-life conditions. It is expected that evolution from one motor state to the other will be observable in the statistics obtained in this work.

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