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Assessment of Bradykinesia in Parkinson's disease patients through a multi-parametric system

M. Pastorino, J. Cancela, M.T. Arredondo, M. Pansera, L. Pastor-Sanz, F. Villagra, M.A. Pastor and J.A Martín

Abstract— **The aim of this paper is to describe and present the results of the automatic detection and assessment of bradykinesia in motor disease patients using wireless, wearable accelerometers. The current work is related to a module of the PERFORM system, a FP7 project from the European Commission, that aims at providing an innovative and reliable tool, able to evaluate, monitor and manage patients suffering from Parkinson's disease. The assessment procedure was carried out through a developed C# library that detects the activities of the patient using an activity recognition algorithm and classifies the data using a Support Vector Machine trained with data coming from previous test phases. The accuracy between the output of the automatic detection and the evaluation of the clinician both expressed with the Unified Parkinson's disease Rating Scale, presents an average value of [68.3±8.9]%. A meta-analysis algorithm is used in order to improve the accuracy to an average value of [74.4±14.9]%. Future work will include a personalized training of the classifiers in order to achieve a higher level of accuracy.**

I. INTRODUCTION

Bradykinesia, one of the main symptoms of Parkinson´s disease (PD), is defined as reduced speed when initiating and executing a single movement and progressive reduction of its amplitude, up to complete cessation during repetitive simple movements [1]. This symptom might represent the most promising motor progression marker of the disease [2]. Bradykinesia appears to result from the inability of PD's patients to maximize their movement speed when required to drive internally their motor output. It has been suggested by Peschel [3] that various aspects appear to contribute to the self-initiation of movements: 1) the selection of movement speed, 2) the selection of the direction of movement, 3) the selection of the kind of movement and 4) the movement timing. In particular, PD'S patients have trouble with movement time. Bradykinesia is caused by the loss of dopaminergic nigrostriatal projections from the substantia nigra pars compacta (SNc) [4][5]. It has been suggested that reduced dopaminergic input to the striatum may result in increased neuronal firing of the inhibitory basal ganglia output and disturbed firing patterns with increased synchronization [5][6][7]. Such changes cause bradykinesia, rigidity, tremor and postural instability, although the underlying mechanisms leading to these symptoms are still not understood [8]. Currently the dopamine precursor levodopa (L-dopa) is the most efficient treatment for the improvement of Parkinson´s disease signs and symptoms. However, abnormal involuntary movements (dyskinesias) are motor fluctuations that occur in the majority of PD's patients undergoing this treatment [9][10]. Thus, excitability abnormalities developing in cortical and subcortical motor networks are currently thought to be the most likely pathophysiological explanation for bradykinesia [11][12]. Based on functional models for the basal ganglia, it has been suggested that hypokinesia may be caused by an abnormally strong inhibition of thalamocortical projections [13][14][15] that decreases the contribution of the basal ganglia to the cortical ''motor set'' energizing of the motor output system [16][17].

The current work is related to "A soPhisticatEd multi-paRametric system FOR the continuous effective assessment and Monitoring of motor status in Parkinson's disease and other neurodegenerative diseases" (PERFORM), within the 7th Framework Programme of the European Commission [18]. It aims at providing an innovative and reliable tool, able to evaluate, monitor and manage patients suffering from motor neurodegenerative diseases. It is composed by a network of wireless accelerometers located on the limbs, trunk and belt of the patient. The software developed selects the best possible combination of sensors and statistical features to relate the output provided by the accelerometers to the Unified Parkinson's Disease Rating Scale (UPDRS) [19] values, used by clinicians to follow the progression of the disease. Developed as a C# library, the prototype accepts an accelerometer signal as input extracts the corresponding features and classifies them according to the knowledge acquired through previous training sessions.

This paper describes the methodology used to assess the severity of Bradykinesia and the results of the tests performed according to the methodology proposed.

II. STUDY DESCRIPTION

A. Subjects and measurement setup

The performance of the bradykinesia severity assessment method was evaluated through several design phases [20].

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M. Pastorino, J. Cancela, M.T. Arredondo, M. Pansera, L. Pastor-Sanz, are with Life Supporting Technologies, Technical University of Madrid (UPM), Madrid 28804 Spain (e-mail: mpastorino@lst.tfo.upm.es, jcancela@lst.tfo.upm.es, mta@lst.tfo.upm.es, mpansera@lst.tfo.upm.es, lpastor@lst.tfo.upm.es,).

F. Villagra and M. A. Pastor are with Division of Neurosciences, Center for Applied Medical Research (CIMA), University of Navarra, Pamplona, Spain. (e-mail: fvillagra@unav.es, mapastor@unav.es).

J.A Martín is with Neurophotonics group, Technical University of Madrid (UPM), Madrid 28804 Spain. (e-mail: jamp@tfo.upm.es).

During the first design phase, data was collected on test patients in a supervised environment, with the collaboration of the medical staff. The dataset used in this study included trials with twenty PD's patients, ten in the University Clinic of Navarra (Spain) and ten in Ioannina University Hospital (Greece), resulting in twenty full cross validations used to train the algorithm and test the method [20]. Each subject performed a supervised protocol both during good clinical status, ON, and during the wearing off efficiency of the medication, OFF status. The patient was requested to carry out daily basic activity (walking, lying on bed, sitting on a chair, drinking a glass of water, opening and closing a door). The described protocols were recorded with a video camera and sensors twice a day while the patient was hospitalized. During each recording, patients were evaluated by a neurologist using the UPDRS scale. TABLE I shows the protocol overview with UPDRS score of the Bradykinesia symptom and the number of recordings carried out, both in ON and OFF phase.

TABLE I
RECORDINGS IN TRAINING PHASE

Bradykinesia UPDRS Score	0	1	2	3	4
Number of recordings	13	27	6	8	2

Once the data has been stored, the processing begins. The first intention is to create a classifier. The steps to achieve this can be described as: 1) selecting the data that corresponds to activities of interest (e.g. walking and arm extension); 2) calculating the resultant vector from the data of each of the three axes; 3) filtering the resultant vector; 4) extracting features and 5) classifying the features. The underlying idea is that the filtered signals contain only the low frequencies, useful to calculate the slow movements of patients. As mentioned, filtered signals were analyzed after running an activity recognition algorithm designed to identify time frames when the patient was either walking or extending/flexing his arms, since bradykinesia is only evident when the patient moves. The signal was then split in 5-second sliding windows with 50% of overlap (epoch), while the features used as input of the classification module were extracted from each epoch. To classify the epochs, different classifiers were used, to find the optimum solution in terms of accuracy and processing time. Range and Root Mean Square (RMS) were the best performing features, after different configuration testing. Regarding the classification method, best results were obtained with the Support Vector Machine (SVM) method. This methodology has been implemented in a C# library.

During the second phase, data was collected in an unsupervised environment and with the collaboration of a caregiver during a week. Data was acquired during an eight-hour daily session in which patients carried out their normal daily activity. Moreover, two daily standard clinical protocol sessions were performed during the trials under the supervision of a clinician. The Neurologist examined the patients distributing the UPDRS twice a day in ON and OFF stages. Subsequently, the protocol sessions were video recorded and matched with the data logger and sensors recordings. During the protocol session the patients carried out the following activities twice a day: sit, read, drink a glass of water and walk for approximately two minutes. At the end of the day, data was processed using the training set computed in the previous phase and the output were checked with the results provided by the clinician, as a result of the evaluation of the standard clinical protocol. This phase included trials with twelve patients in Pamplona (Spain).

B. System for data collection

The wearable device used to recording the accelerometer signals consists of a tri-axial accelerometers' set used to record the accelerations of the movements at each patient limb, one accelerometer and gyroscope (on the belt) used to record body movement accelerations and angular rate, and a data logger that receives and stores all recorded signals in a SD card. Sensors were placed in every limb and belt to allow the system detecting and quantifying a wide range of symptoms and measures of Parkinson's disease patient i.e. tremor, bradykinesia, dyskinesias and freezing of gait. All sensors transmit data using Zigbee protocol to a logger device, with 62.5 Hz sampling rate (16 milliseconds between samples).

Once the data has been stored in the SD card, the Local Base Unit (LBU) is responsible for the identification and quantification of the patient symptoms and the recording of other useful information for the evaluation of the patient status. The LBU receives patient signals and detects the targeted patient symptoms. For each symptom, a dedicated submodule processes the relevant signals, detects the symptom episode and quantifies it into a severity scale from 0 to 4, according to the UPDRS scale for PD's patients.

C. Patients data

Patients fulfilling the following criteria were eligible for the study: diagnosis of Parkinson's disease, aged between 40-75 years old, ambulatory and capable of complying with study requirements, receiving stable dopaminergic treatment, experiencing motor fluctuations and presence of a responsible caregiver who can cooperate with the patient and his/her neurology specialist. The exclusion criteria for this study were suffering from dementia, psychosis (simple visual hallucinations excluded) or a significant systemic disease (such as: cancer, hepatic or kidney dysfunction, etc.).

During the second phase of the trials, twenty-four PD's patients were selected (6 women and 18 men) with an age between 52 and 79 years old (mean 62.77± 6.5 years).

D. Experimental Setup

The aim of the experiment was to test the algorithms previously developed in an uncontrolled environment. In order to achieve this goal, the patients were asked to wear the sensors at home during a week. The devices were pre-programmed to continuously monitor the patient for 8 hours every day. The patient had to wear the devices in the morning, and had to switch them on 10 minutes before the start of the pre-scheduled monitor session. The patient was then free to carry out his/her usual daily activities. During the day the patient had to introduce the information about the medication intake and the meal intake, using the

patient's GUI. At the end of the day the patient had to connect the device to the PC, where the downloading and signal processing started automatically. A caregiver was trained to help and assist the patient during the recordings. Two daily visits from the clinician to the patient's home took place in order to evaluate the patient's status.

In order to test the algorithms previously developed, six PD's patients from University Clinic of Navarra (Spain) were selected (2 women and 4 men) with an age between 63 and 68 years old (mean 64.63 ± 2.25 years).

III. Methodology

A. System description and classification method

During the first phase of the PERFORM project, an intelligent system, that monitors the motor signals of the patients, was developed in order to detects the symptoms episodes and quantify them into a severity scale from 0 to 4, according to the UPDRS scale for PD's patients.

The second phase aimed at testing the patient-side subsystem called Local Based Unit (LBU) and comparing the output with the annotation of the medical stuff. Once data is stored in the patient device the signal process starts automatically. Different modules were created in order to detect and quantify different symptoms as shown in Fig. 1.

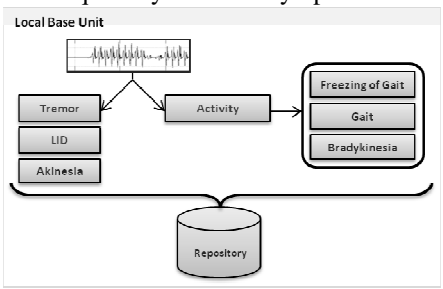

Fig. 1 Signal process schema of LBU

In order to assess the bradykinesia severity, an algorithm for activity recognition has been implemented to select the movement events. Then Range and RMS features are extracted from the signals acquiring from the limbs sensors. Finally a SVM classifier, trained with data collected from the previous phase is used to quantify the severity of the processed epoch [20]. Once all classifiers are run the output was stored inside a local repository. TABLE II shows an example of the Bradikynesia output. Every line corresponds to a classified 5-second interval (epoch).

TABLE II
BRADYKINESIA OUTPUT EXAMPLE

Start Time	End Time	Severity	Certainty	Overlap
2011-02-08 15:42:33:658	2011-02-08 15:42:38:633	1	66.77%	50
2011-02-08 15:42:36:154	2011-02-08 15:42:41:129	1	89.47%	50

The output format includes the severity of the Bradikynesia, computed in the interval between start time and end time as the result of the classification. The certainty is a combination between the classifier probability and the movement certainty. The first one indicates the grade of relationship between the value and the associated hyperplane, while the second one indicates the certainty of movement during the epoch. The last column contains the overlap value, in this case 50%. This value is useful to rebuild the timeline.

B. Accuracy of classifiers

Once all signals are processed, the output is compared with the clinician annotation in order to define the accuracy of the classifiers, expressed as the percentage of epochs that matches with the clinician annotation during the test.

C. Meta-analysis algorithm

The goal of the meta-analysis algorithm is to take the epoch and detect events, transition periods and remove "noise" from the output. The new UPDRS value is calculated using both UPDRS values and the certainty values. Actually for each time slot there is information from two different sources which provides more information than only one. Hence, given a timeslot it is possible to merge the information from two epochs using a weighted sum; the new value will take the information from the UPDRS values and certainty values. Then, the algorithm will find the closest UPDRS value to the output provided by the classifiers and this value will be assigned to the current time slot.

IV. Results

The values of the accuracy show that there is a strong correlation between the clinician evaluation and the severity detected by the Bradikynesia classifier. During a week and twice a day, a visit from the clinician to patient's home took place in order to perform UPDRS evaluation. The portion of the signal recorded during the evaluation was used to the comparison between clinician evaluation and the output of the classifier. TABLE III shows the results of this test phase with six patients from Clinica Universitaria de Navarra.

TABLE III
RESULTS OF PROCESSED DATA

	Annotated Epochs	Correct Epochs	Accuracy [Mean±Std.Dev]	Accuracy [Max]	Accuracy [Min]
Patient A	134	84	[53.4±17.9]%	86.7%	37.5%
Patient B	78	53	[65.7±9.4]%	80.9%	58.3%
Patient C	126	95	[70.93±16.3]%	100%	52.9%
Patient D	38	25	[68.1±16.2]%	87.5%	56.3%
Patient E	91	67	[78.1±20.3]%	100%	42.9%
Patient F	277	218	[76.5±4.9]%	83.3%	69.4%
TOTAL	744	542	[68.3±8.9]%	78.1%	53.4%

The annotated epochs column reports the generated movement epochs during the tests, while the Corrected Epochs column defines the number of epochs that coincide with clinician annotation. The accuracy column defines the average accuracy computed during the UPDRS evaluation along the week. The last two columns show the maximum and minimum values of the accuracy. The last row is the summary of the results of the week evaluation. The results show that the global outputs of the bradykinesia classifier are in agreement with the medical evaluation. The lowest values of accuracy could be caused by the use of a different

methodology evaluation between the classifier and the clinicians. The classifier computes the value of the Bradikynesia every 5 seconds using only the motor behavior information while the evaluation of the clinician is defined as the global slowness of movement during the daily visit.

In order to improve the results of the output classifier, an algorithm for meta-analysis is used. TABLE IV shows the results of six PD's patients using the meta-analysis algorithm. The aim of this algorithm is to smooth the peak generation during the processing. These peaks introduce an error in the overall evaluation of the accuracy during the acquisition period. An overall comparison between the results of TABLE III and IV shows that the accuracy of the classifier outputs increases when the meta-analysis algorithm is applied. The mean accuracy value only decrease in the case of Patient A, this could be caused by the variability of the bradykinesia symptom in the patient. However the results of TABLE IV show that the Bradikynesia classifier reaches a highest value of maximum accuracy when the meta-analysis algorithm is applied.

TABLE IV
RESULTS OF PROCESSED DATA WITH META-ANALYSIS ALGORITHM

	Annotated Epochs	**Correct Epochs**	**Accuracy [Mean±Std.Dev]**	**Accuracy [Max]**	**Accuracy [Min]**
Patient A	134	86	[48.8±30.3]%	92.9%	20.0%
Patient B	78	62	[83.5±3.2]%	85.7%	81.3%
Patient C	126	104	[78.1±17.6]%	100%	50%
Patient D	38	26	[70.9±23.3]%	100%	57.1%
Patient E	91	70	[82.1±22.3]%	100%	42.9%
Patient F	277	254	[91.9±6.7]%	100%	75.0%
TOTAL	744	602	[74.4±14.9]%	91.9%	48.8%

V. CONCLUSION

The proposed system provides a useful tool for the analysis of the bradykinesia in PD's patients. The large variability and the unpredictability of the movement may be the cause of classification errors. In fact it is complicated to find a common pattern in different PD's patients in an unsupervised environment. The results of the second phase of testing are satisfactory, reaching a high level of accuracy, taking in account that evaluation of the status of the patient by clinicians presents a statistical error of 5% due to the subjective characteristics of the UPDRS scale. The test–retest reliability of the motor UPDRS in patients with PD's has excellent test–retest reliability, with an interclass correlation coefficient (ICC) of 0.90 [21].

To confirm and improve these initial results, not only the testing phase will continue on a larger sample of patients, but the classification method will also need to be personalized, in order to achieve a higher level of accuracy, for example introducing special classifier trained for each patient in order to adjust the parameters.

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REFERENCES

[1] Wilson SAK. Disorders of motility and tone. Lancet 1925; 206: 1–10, 53–62, 169–78; Marsden CD. The mysterious motor function of the basal ganglia: the Robert Wartenberg Lecture. Neurology 1982; 32: 514–39

[2] W. Maetzler, I. Liepelt and D. Berg Progression of Parkinson's disease in the clinical phase: potential markers. Lancet Neurol. 2009 Dec;8(12):1158-71

[3] T. Peschel, H.J. Heinze and M. Rotte. (2006). "Increased pre-SMA activation in early PD patients during simple self-initiated hand movements".

[4] R.L. Albin, A.B. Young and J.B. Penney "The functional anatomy of basal ganglia disorders", Trends Neurosci 1989; 12: 366–75.

[5] M.R. DeLong, "Primate models of movement disorders of basal ganglia origin". Trends Neurosci. 1990 Jul;13(7):281-5. Review.

[6] R. Levy, W.D. Hutchison, A.M. Lozano and J.O. Dostrovsky "Synchronized neuronal discharge in the basal ganglia of parkinsonian patients is limited to oscillatory activity". J Neurosci 2002; 22: 2855–61.

[7] P. Brown, "Oscillatory nature of human basal ganglia activity: relationship to the pathophysiology of Parkinson's disease", Mov Disord 2003; 18: 357–63.

[8] I.A. Prescott, J.O. Dostrovsky, E. Moro, M. Hodaie, A.M. and W.D. Hutchison, "Levodopa enhances synaptic plasticity in the substantia nigra pars reticulata of Parkinson's disease patients", Brain. 2009 Feb;132(Pt 2):309-18. Epub 2008 Dec 2.

[9] J.A. Obeso, C.W. Olanow and J.G. Nutt, "Levodopa motor complications in Parkinson's disease", Trends Neurosci 2000a; 23: S2–7.

[10] J.A. Obeso, M C. Rodriguez-Oroz, M. Rodriguez, J.L. Lanciego, J. Artieda, N. Gonzalo, et al. "Pathophysiology of the basal ganglia in Parkinson's disease", Trends Neurosci 2000b; 23: S8–19.

[11] M. Hallett and S. Khoshbin, "A physiological mechanism of bradykinesia". Brain 1980;103:301–314.

[12] A. Berardelli, A.F Sabra and M. Hallett, "Physiological mechanisms of rigidity in Parkinson's disease", J Neurol Neurosurg Psychiatry 1983; 46:45–53.

[13] F. Blandini, G. Nappi, C. Tassorell and E. Martignoni, "Functional changes of the basal ganglia circuitry in Parkinson's disease", Prog Neurobiol 2000;62:63–88.

[14] M.R. DeLon and T. Wichmann, "Circuits and circuit disorders of the basal ganglia", Arch Neurol 2007;64:20–24

[15] H. Braak and K. Tredici, "Cortico-basal ganglia-cortical circuitry in Parkinson's disease reconsidered", Exp Neurol 2008;212: 226–229.

[16] A. Pascual-Leone, J. Valls-Sole, J.P. Brasil-Neto, L.G. Cohen and M. Hallett, "Akinesia in Parkinson's disease. I. Shortening of simple reaction time with focal, single-pulse transcranial magnetic stimulation". Neurology 1994;44:884–891.

[17] R. Chen, S. Kumar, R.R. Garg and A.E. Lang, "Impairment of motor cortex activation and deactivation in Parkinson's disease", Clin Neurophysiol 2001;112:600–607.

[18] PERFORM project (IST- 215952) Annex I- Description of Work 2007

[19] Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease. The Unified Parkinson's Disease Rating Scale (UPDRS): Status and Recommendations. Movement Disorders Vol. 18, No. 7, 738-750 (2003)

[20] J. Cancela, M. Pansera, M.T. Arredondo, J.J. Estrada, M. Pastorino and L. Pastor-Sanz, "A comprehensive motor symptom monitoring and management system: the bradykinesia case". Conference proceedings of Annual International Conference of the IEEE Engineering in Medicine and Biology Society, pp. 1008-11. 2010, August 31 – September 4.

[21] A. Siderowf, M. McDermott, K. Kieburtz, K. Blindauer, S. Plumb and I. Shoulson, "Test-retest reliability of the unified Parkinson's disease rating scale in patients with early Parkinson's disease: results from a multicenter clinical trial", Mov Disord. 2002 Jul;17(4):758-63.