A Long-Term Monitor Including Activity Classification for Motor Assessment in Parkinson's Disease Patients

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Abstract — **Tremor and bradykinesia are two prominent features of Parkinson's disease (PD). Currently, these motor symptoms are evaluated by physicians, generally using the Unified Parkinson's Disease Rating Scale (UPDRS). In addition to these short subjective physician's tests, it is desirable to develop an objective, ambulant system thoroughly assessing tremor and bradykinesia accurately over long-term.**

This paper presents the PD monitor, a measurement system using accelerometry to quantify tremor and bradykinesia. For the evaluation of tremor, rest tremor in the arm, thigh, and trunk and kinetic tremor in the arm were quantified. Bradykinesia was assessed by parameters related to arm movement, walking, and standing up. An Activity Classifier was integrated, enabling a more detailed analysis than currently available systems.

The PD monitor was validated using measurements of six PD subjects receiving deep brain stimulation in the subthalamic nucleus. During the experiments, each patient wore four sensors while subsequently receiving three different stimulation settings: stimulator on, stimulator on at 80% of the normal stimulation amplitude, and stimulator off. Concurrently, patients were recorded on video, which were rated by a physician using the UPDRS.

A correlation analysis of the physician's scores and the PD monitor demonstrated that the system accurately measured the severity of tremor and bradykinesia whilst assessing a broad spectrum of aspects related to both symptoms.

In conclusion, the PD monitor can be used for a detailed evaluation of the PD motor symptoms in order to optimize treatment.

Keywords — **Ambulatory monitoring, Activity monitoring, Tremor, Bradykinesia, Parkinson's disease**

I. Introduction

Parkinson's disease (PD) is a disorder impairing motor skills, resulting in symptoms such as tremor and bradykinesia. Tremor is a symptom which induces rhythmic involuntary movements in arms, legs, trunk and/or head. It may occur during both rest and movement. In this paper, bradykinesia is defined as the inability to move and the slowness of movement. Bradykinesia leads to reduced arm movement, slowness of walking, reduced arm swing during walking, and difficulty in standing up.

Currently, PD is assessed by short subjective tests performed by a physician. The Unified Parkinson's Disease Rating Scale (UPDRS) is one of the most commonly used standards. Drawbacks are its subjectivity, observation during short periods of time only, and unfamiliarity of the environment during the observation. To overcome these shortcomings, an objective system, which is able to perform ambulant long-term measurements, is desirable.

Ambulant measurement of tremor and bradykinesia is widely studied [1-4]. However, the reported analyses usually incorporate only general aspects, while the symptoms are actually more complex. Rest and kinetic tremor are two independent symptoms [5,6], but they are usually treated as a single, combined symptom. Similarly, research often concentrates on arm tremor, although other body parts may suffer from tremor independently. Furthermore, bradykinesia is commonly assessed by looking at the amplitude and duration of arm movement, even though difficulties with standing up and walking are essential too. Salarian et al. [3] analyzed transitions and gait in more detail, but studied these parameters separately.

This paper presents the PD monitor, a system that is able to objectively analyze tremor and bradykinesia ambulant, and over long periods of time. Furthermore, it assesses all aspects of these symptoms in detail. To enable a thorough evaluation, all these aspects were integrated into a comprehensive analysis system, which included an Activity Classifier (AC). In the PD monitor, the AC was included to enable a detailed assessment of tremor and bradykinesia, which has not been done before. An AC has been used before [3], but was applied to detect on and off periods.

In this paper, the accuracy of the PD monitor is demonstrated and it is shown that it may be used to optimize treatments.

II. Methods

A. Experiment setup

Six PD patients (age 61.5±4.5) took part in the experiments approved by the local Medical Ethics Committee. For inclusion, PD patients had to:

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1. receive deep brain stimulation (DBS) in the subthalamic nucleus
2. show good clinical results by DBS
3. respond within five minutes to changes in stimulator settings
4. be able to fully cooperate with the experiments
5. have no major symptom fluctuations due to medication
6. not suffer from dementia
7. not suffer from dyskinesia

As a control group, seven healthy subjects (age 57±2.6) were measured.

During the experiments, each subject wore four inertial sensors (MT9®, Xsens Technologies BV, Enschede, the Netherlands). The PD monitor used the 3D acceleration of all sensors and the angular velocity measured axially on the foot. All signals were measured at a sample frequency of 50 Hz. The inertial sensors were placed on the trunk and wrist, thigh, and foot of the most affected side. The sensors were wired to the Xbus master, which transferred information to a laptop via Bluetooth. The subject was videotaped, and the tapes were used by the physician to rate the UPDRS, while being blind to stimulator settings.

After the sensor-calibration, each subject had to perform certain sets of movement tasks comprising daily activities and UPDRS tests. The daily activities included walking, standing, sitting, lying, standing up, drinking a glass of water, and moving a bottle. The UPDRS-III (motor examination) tests 20, 21, 23 to 27, 29 and 31 were performed [5]. The set of movement tasks was performed in a predetermined random order.

The subjects were measured under three conditions, received in a predetermined, random order. The conditions were: 1) Stimulator on having optimal settings (determined by physician), 2) Stimulator on having a stimulation amplitude at 80% of the optimal value, and 3) Stimulator off. One patient was not measured during condition 3, because of severe dyskinesias occurring with stimulator off.

B. Data analysis

Preprocessing: First, the raw motion signal of the sensor was retrieved (figure 1). To study body movements, this signal had to be converted from the sensor to the body coordinate frame. Hence, rotation matrices were developed using solely acceleration data, applying a method similar to the one described by Luinge et al. [7]. The signal in the body frame was filtered below 23 Hz to reduce noise. Subsequently, the signal was low-pass filtered using a second order Butterworth filter at 0.25 Hz to obtain the orientation signal. To retrieve the movement signal, the orientation signal was subtracted from the original signal.

Activity Classifier (AC): The AC was based on a decision tree. First, certain features were extracted from the signal (figure 1). Subsequently, the decision tree classified the activity of each one-second window using the previously extracted features. The defined activities were walking, standing up, lying, standing with and standing without active arm movement (AAM), and sitting with and sitting without AAM. The activities classified by the AC were compared to manually labeled data using video recordings. Subsequently, the accuracy (the ability to correctly classify each window), specificity (the ability to not generate false detections), and sensitivity (the ability to detect the true positives) were computed.

Motor Symptom Monitor (MSM): The activity-classified signal was processed further in the MSM (figure 1). Again, features were extracted from the signal. The type of feature and thresholds depended on the previously detected activity. For example, when the AC classified sit with AAM (figure 2), the average arm acceleration (figure 3) was computed.

Tremor analysis was subdivided into a detection and quantification part. First, tremor detection was performed. Thresholds for tremor detection were defined by a training procedure in which training and test data were strictly separated using the leave-one-subject-out method. The trained thresholds were different per activity and body segment, because tremor may be expressed differently during different activities and in different limbs [5].

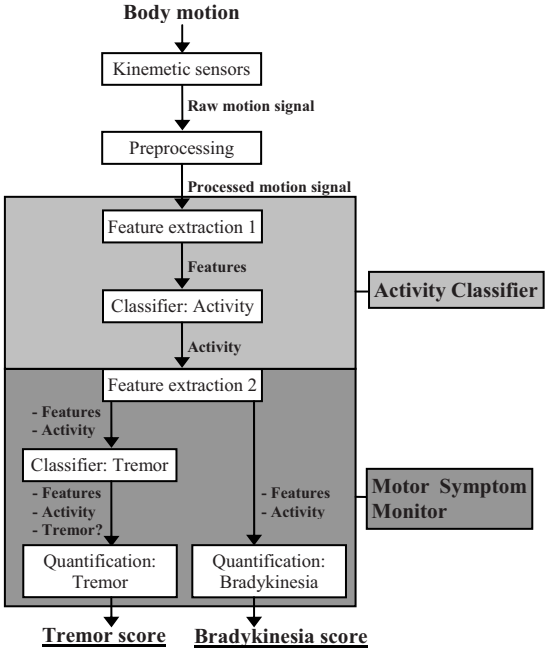

Fig. 1 A schematic representation of the PD monitor.

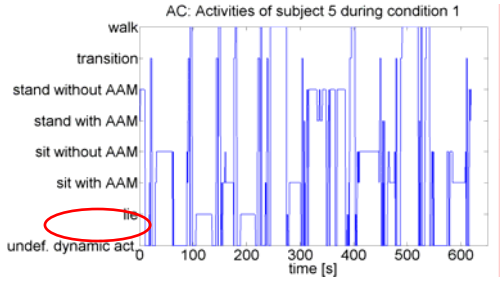

Fig. 2 *AC*: The activities of subject 5 during condition 1.

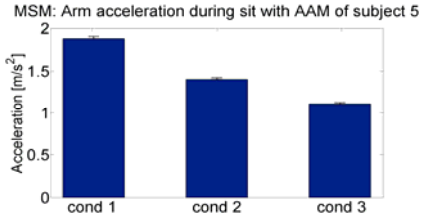

Fig. 3 *MSM*: The average arm acceleration, representing bradykinesia, within different conditions for subject 5. This parameter was computed when sit with AAM (figure 2) was detected. Error bars are included.

Detection of tremor was done per three-second window during sitting and standing. Arm rest tremor was analyzed during periods without AAM, while arm kinetic tremor was detected during periods with AAM. For the thigh and trunk, only rest tremor was assessed. Different algorithms were used for rest and kinetic tremor detection. To detect rest tremor, the 3D acceleration was first filtered between 3.5 and 9 Hz using a second order Butterworth filter. Subsequently, the data of each axis was multiplied by a three-second Blackman window. The window was slid over the data per second. Different frequency ranges for filtering and the use of a rectangular window were assessed, but provided poorer results. Subsequently, each window was Fourier transformed. The resulting frequency plot was analyzed for its dominant frequency peak. Rest tremor was detected, when the power of the dominant peak exceeded a threshold. For kinetic tremor detection, filtering and windowing were identical to the approach for rest tremor, but using a frequency range of 3.5 to 12 Hz. Next, the detection algorithm for kinetic tremor concentrated on the fact that one's individual tremor usually occurs in a small frequency band. As the frequency plot is also influenced by non-tremor movement, this characteristic was important. For this purpose, a periodogram was computed per window. From this graph, a second order moment was calculated, which represents the frequency bandwidth of the signal around the mean frequency. Kinetic tremor was detected when a small second order moment was found.

Rest tremor-labeled data was quantified using several combinations of tremor duration and tremor amplitude in three directions. Kinetic tremor was quantified by the duration of tremor, because the amplitude was influenced by normal movement too much. For both types of tremor, values were computed separately for sitting and standing.

Several aspects of bradykinesia were considered. First, the slowness of movement was assessed by computing the amplitude of arm movement. This was done by computing the root mean square value of the 3D acceleration. Second, the percentage of time during which the arm was active was used as a measure for the poverty of movement. The third aspect was the difficulty with walking. For this, step length, step velocity, variation in step length, and arm swing were computed. Step length and velocity were computed using the 3D acceleration and axial angular velocity on the foot. This was done by a previously validated method of Sabatini et al. [8]. Step length and velocity were normalized by leg length. Arm swing during walking was assessed by examining the correlation between the low-pass filtered (<1 Hz) acceleration components of the wrist and thigh sensor. Finally, troubles during standing up were assessed by the low-pass filtered trunk acceleration signal (<0.65 Hz), representing orientation change in the trunk. The transition duration was computed, as well as the minimal trunk acceleration. Additionally, the range of trunk acceleration was determined.

The correlation of the PD monitor's output and the UPDRS scores were computed. Additionally, the parameters were compared per condition using a one-way RM ANOVA and subsequent Tukey test.

III. Results

Activity Classifier: The activity classification by the AC (example of one trial is given in figure 2) was very accurate. When analyzing the data of PD patients, the overall accuracy was 98.8%, the sensitivity was 94.3%, and the specificity was 99.3%. The AC was also trained and evaluated using data of healthy subjects. Results were slightly better for this group, showing an overall accuracy of 99.3%, sensitivity of 96.8%, and specificity of 99.6%.

Motor Symptom Monitor: The best correlations for rest tremor were obtained for: tremor amplitude*duration^{½} (instead of the duration to the power ¼, ¾, or 1). Rest tremor in the arm was quantified best when computing data in the axial and radial direction measured during stance. This provided a correlation of 0.86 to UPDRS 20. For thigh rest tremor, the acceleration in the tangential direction during sitting provided the highest correlation, viz. 0.90. The physician did not score trunk tremor, as this is not done in a standard UPDRS test. Finally, the correlation between kinetic arm tremor during sitting and UPDRS 21 was 0.73.

Table 1 The evaluation of bradykinesia

Activity	MSM-Parameter	Correlation
Transition	duration (s)	0.64
	minimal acceleration (m/s^2)	-0.67
	range of acceleration(m/s^2)	-0.64
Walking	correlation thigh vs. arm movement	-0.52
	step length	-0.68
	step length variation	n.s.
	step velocity	-0.69
With AAM	sit average arm movement	-0.77
	stand average arm movement	-0.73
With and without AAM	sit average arm movement	-0.70
	stand average arm movement	n.s.
	sit % of movement time	n.s.
	stand % of movement time	n.s.

n.s. = not significant
AAM = active arm movement

When comparing tremor severities during different conditions, it was shown that normalized arm, thigh, and trunk rest tremor differed significantly between all conditions, and *P*-values of 0.039, 0.011, and 0.007 were obtained respectively. The post-hoc Tukey test revealed significant differences between stimulator on and off (*P*-values: 0.032, 0.021, and 0.006 for the arm, thigh, and trunk). Furthermore, significant differences between stimulator on having altered settings and stimulator off were achieved (*P*-values: 0.016 and 0.044 for the thigh and trunk). Finally, kinetic tremor analysis gave no significant differences, but the expected trends were observed. Tremor increased as the condition deteriorated.

For bradykinesia, correlating output parameters with UPDRS score 31 were found for all aspects, viz. transitions, walking, and arm movement (table 1). Parameters measured during sitting correlated better. The objective parameters for bradykinesia were not significantly different between different conditions. However, the powers of the tests were too low. Still, the expected trends were observed, i.e. bradykinesia worsened as the condition deteriorated. Figure 3 shows the decrease of average arm acceleration during sitting with AAM as the condition deteriorates in subject 5.

IV. Discussion

Currently, treatment of PD is optimized based on several short evaluations by the physician. Severity of symptoms are rated using the UPDRS. The PD monitor is an objective alternative, which is capable of measuring ambulant over a long period of time. Current objective systems usually only measure general aspects of symptoms like tremor and bradykinesia, while they actually encompass a range of aspects. The PD monitor accomplishes a detailed analysis by incorporating an Activity Classifier.

This paper shows that the PD monitor is able to produce objective measures that correlate well to UPDRS scores of the physician. Additionally, the objective measures cover a wide range of aspects related to tremor and bradykinesia. Furthermore, it is demonstrated that the PD monitor is able to discriminate severity of symptoms during different levels of treatment. For tremor parameters, these differences were statistically significant. In contrast, the good-correlating kinetic tremor and bradykinesia parameters showed the expected trends, but did not differ significantly. However, the power of the performed tests was too low. Furthermore, inter-individual differences made it difficult to find significant differences.

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References

1. Dunnewold R.J.W., Jacobi C.E., van Hilten J.J. (1997) Quantitative assessment of bradykinesia in patients with Parkinson's disease. J Neurosci Meth 74:107–112
2. Hoff J.I., Wagemans E.A., van Hilten J.J. (2001) Ambulatory objective assessment of tremor in Parkinson's disease. Clin Neuropharmacol 24:280–283
3. Salarian, A. (2006) Ambulatory monitoring of motor functions in patients with Parkinson's disease using kinematic sensors. École Polytechnique Fédérale de Laussanne, Lausanne
4. van Someren E.J.W., Pticek M.D., Speelman J.D. et al. (2006) New actigraph for long-term tremor recording. Mov Disord. 21:1136-1143
5. Fahn S., Elton R.L., members of the UPDRS Development Committee (1987) Unified Parkinson's Disease Rating Scale. In: Fahn S., Marsden C.D., Calne D., et al., eds. Recent Developments in Parkinson's Disease, vol **2**. Macmillan Healthcare Information, Florham Park, NJ
6. Kraus P.H., Lemke M.R., Reichmann H. (2006) Kinetic tremor in Parkinson's disease – an underrated symptom. J Neural Transm 113:845-853
7. Luinge H.J., Veltink P.H, Baten C.T.M. (2007) Ambulatory measurement of arm orientation. J Biomech 40:78-85
8. Sabatini A.M., Martelloni C., Scapellato S., et al. (2005) Assessment of walking features from foot inertial sensing. IEEE T Bio-Med Eng 52:486-494

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