Ambulatory Monitoring of Activities and Motor Symptoms in Parkinson's Disease

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***Abstract*—Ambulatory monitoring of motor symptoms in Parkinson's disease (PD) can improve our therapeutic strategies, especially in patients with motor fluctuations. Previously published monitors usually assess only one or a few basic aspects of the cardinal motor symptoms in a laboratory setting. We developed a novel ambulatory monitoring system that provides a complete motor assessment by simultaneously analyzing current motor activity of the patient (e.g., sitting, walking, etc.) and the severity of many aspects related to tremor, bradykinesia, and hypokinesia. The monitor consists of a set of four inertial sensors. Validity of our monitor was established in seven healthy controls and six PD patients treated with deep brain stimulation (DBS) of the subthalamic nucleus. The patients were tested at three different levels of DBS treatment. Subjects were monitored while performing different tasks, including motor tests of the Unified PD Rating Scale (UPDRS). Output of the monitor was compared to simultaneously recorded videos. The monitor proved very accurate in discriminating between several motor activities. Monitor output correlated well with blinded UPDRS ratings during different DBS levels. The combined analysis of motor activity and symptom severity by our PD monitor brings true ambulatory monitoring of a wide variety of motor symptoms one step closer.**

***Index Terms*—Activity classification, ambulatory monitoring, bradykinesia, Parkinson's disease (PD), tremor.**

I. Introduction

PARKINSON'S disease (PD) motor symptoms mainly consist of progressive bradykinesia, tremor, hypokinesia, rigidity, and impaired postural control. The patients are usually treated with drugs, but some are additionally treated with deep brain stimulation (DBS). To optimize therapies, it is essential to know how much the symptoms are suppressed by treatment. Currently, the specialist assesses the effect on the symptoms by taking the history and by performing clinical examinations (e.g., the Unified PD Rating Scale – UPDRS). These procedures cover only a short episode of the patient's condition, in spite of the fact that symptoms often fluctuate significantly within and between days. Patients sometimes keep diaries to record motor fluctuations, but these are subjective and influenced by subject inaccuracies. Clinical observation of fluctuations by medical staff is time consuming and not always representative since the clinical environment is unfamiliar and sometimes rather stressful to the patient. In addition, the demand on healthcare is growing rapidly, i.e., the number of PD patients worldwide is predicted to increase from 10 million in 2000 to 40 million patients in 2020 [1]. For these reasons, an objective monitor performing both long-term and ambulatory measurements of symptom severity is needed.

Ambulatory monitoring of PD, studying tremor, bradykinesia, and hypokinesia with kinematic sensors has been widely studied over the past decades [2]–[5]. However, these studies usually only consider a few basic aspects of the complex symptomatology. When assessing tremor, rest and kinetic tremor should be treated as separate phenomena [6], [7]. Nevertheless, in previous studies they are usually quantified as a single symptom. In addition, only rest tremor in the arm is commonly evaluated, even though tremor in the leg and upper body can also be significant in PD [6]. Bradykinesia and hypokinesia are generally assessed by looking at arm activity. These symptoms, however, also impair walking, and cause decreased step length and velocity, increased variation in step length, and reduced arm swing. Another major problem in PD patients is standing up from a sitting position. Thus far, only Salarian [5] has attempted to use additional measures retrieved during posture transitions.

The PD monitor, presented in this paper, is able to perform both long-term and ambulatory measurements to assess patients objectively. Whereas previous monitors only assess a few aspects of motor symptoms, our PD monitor performs a detailed analysis of multiple symptoms and provides a complete assessment of tremor, bradykinesia, and hypokinesia. On top of that, the use of an activity classifier (AC) within a PD monitor is proposed to differentiate between lying, sitting, standing, standing up, and walking. This enables the complete analysis of motor symptoms and the possibility for direct implementation into an ambulatory environment. The AC is essential for these applications: For instance, to compute step length, the activity ''walking'' should be classified first. In addition, when an activity without arm movement is detected, rest tremor in the arm can be evaluated, but when arm movement is detected, kinetic tremor can be evaluated.

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The AC has hardly been studied in combination with the PD monitors, even though it is essential for a complete ambulatory assessment. Salarian [5] incorporated an AC into a PD monitoring system, but used it only for the determination of on and off periods. In addition, Dunnewold *et al.* [10] used an AC, but they only considered static activities and they assessed just a few basic aspects of PD motor symptoms. In contrast, the AC itself has been a subject of research for a long time [8]–[14]. Methods have been proposed for the discrimination of static from dynamic activities using the alternating current component of an acceleration signal [8], [9]. Within the static activities, posture detection can be performed by assessing the direct current component of the acceleration signal [8], [10]. Considering dynamic activities, it has been proposed that detection of walking is possible by analyzing signal morphology [8], peak detection [11], or the frequency domain entropy [12].

In this paper, we studied a new ambulatory monitoring system that combines several algorithms to classify current motor activity and symptom severity simultaneously. This combined detection of motor activity and symptom severity yields a monitor that is truly ambulatory, in a way that it provides easily interpretable data even when used in the patient's home environment. A preliminary version of this paper has been reported [15].

II. Method

A. Experimental Setup

Six PD patients (age 54–68) treated with DBS in the subthalamic nucleus took part in the experiments. We chose to use patients with DBS in order to test whether our PD monitor was responsive to instantaneous changes in symptom severity within subjects. Patients were included when they had good clinical results with DBS and responded within 5 min to changes in stimulator settings. Furthermore, they had to be able to fully cooperate with the experiments, show no major symptom fluctuations due to medication, and not suffer from dementia or dyskinesias. As a control group, seven healthy subjects (age 53–61) were also included. The study protocol was approved by the local medical ethical committee and all subjects gave written informed consent after a thorough written and oral explanation of the experimental setup.

The patients were measured under three conditions. Condition 1 ("on"): Stimulator at the optimal settings (as determined previously by the treating physician). Condition 2 ("intermediate"): Stimulator at a stimulation amplitude of 80% of the optimal setting. Condition 3 ("off"): Stimulator off. The measurements started 15–30 min after the adjustment of the DBS. The healthy control group was measured in one condition, their healthy state. During each condition, the subject was asked to perform certain daily tasks and UPDRS motor tests in a randomly predefined order. Each task was repeated two times, except for the tasks related to standing up. These tasks were each repeated three times. The daily tasks included: sitting quietly for 30 s; sitting while rapidly tapping three predefined spots forming a triangular shape on a table using the most affected arm for 20 s; transition from sitting to standing (UPDRS motor score item 27); transition from sitting to standing and walking (the timed-up-and-go test); walking for 30 s (UPDRS item 29); standing still for 30 s; standing while picking up, drinking, and returning a cup of water; standing while moving a bottle of water from one spot to another; lying down on a bed for 30 s. In addition, the following UPDRS-III motor tests were assessed: rest tremor of the arm and leg (UPDRS item 20); postural tremor of the arm (UPDRS item 21) and kinetic tremor while touching the nose and researcher's index finger alternately using the most affected arm; rapid pronating and supinating movements for 20 s (UPDRS item 25); foot tapping for 20 s (UPDRS item 26).

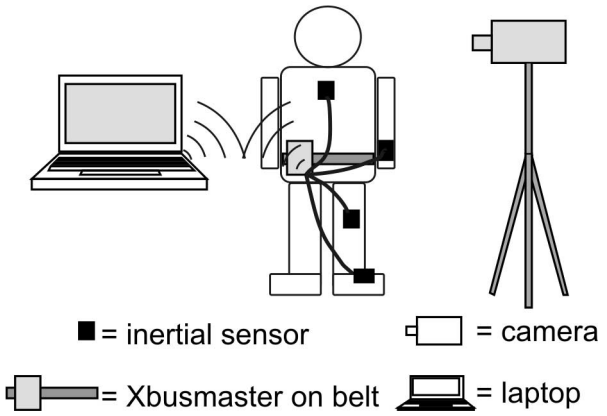

Fig. 1. Schematic representation of the experimental setup. The subject wore four inertial sensors placed on the wrist, thigh, and foot of the most affected site and on the sternum. The sensors were wired to the ''Xbus master," which provided power, collected, and sent data to the laptop via bluetooth. The patient was also videotaped.

During all these tasks, motor activity was measured using four MT9 inertial sensors (3-D accelerometers and 3-D gyroscopes, Xsens Technologies BV, Enschede, The Netherlands). The sensors were placed on the trunk and wrist, thigh, and foot of the most affected side of patients and the dominant side of the control group (see Fig. 1). A 50 Hz sample frequency was used. The Xbus master, worn around the waist, sent the data from the sensors to a laptop via bluetooth. The activities of the subject were videotaped. The video recording was of a satisfactory quality, i.e., resolution of 720×576 pixels and a rate of 25 frames/second [16]. Using this video, actual activities were visually determined as a gold standard to which the PD monitor's AC output was compared. The physician, who was blind to stimulator settings, also used this recording to score a subset of the UPDRS [6] during each of the three conditions. Louis *et al.* [17] showed that videotaped UPDRS motor examination is a sufficiently accurate alternative to in field studies.

B. Data Analysis

Our PD monitor used a three-step approach. First, the raw signal was preprocessed. Second, the AC evaluated the current motor activity of the patient for each measured second (e.g., sitting still, sitting while moving the arm, standing, etc.). Third, the motor symptom monitor (MSM) determined the severity of the motor symptoms, i.e., tremor, bradykinesia, and hypokinesia. Fig. 2 shows the general structure of the PD monitor. The

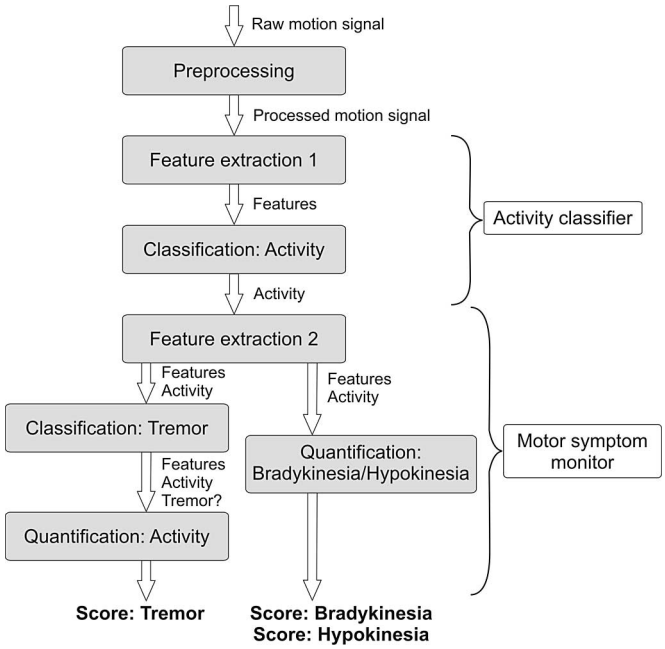

Fig. 2. General structure of the PD monitor. Body motion is measured by the inertial sensors and the raw motion signal is preprocessed. The AC first extracts features, which are used by the classifier to determine the activities (see Fig. 3). After the AC, the information is split into two data streams of the MSM, one for tremor and one for bradykinesia and hypokinesia. Dependent on the activity, certain features are extracted and tremor detection is performed. When tremor is present, the tremor severity is determined (see Fig. 4). In the second data stream, bradykinesia and hypokinesia severity are determined (see Fig. 5).

next three paragraphs describe each step of the PD monitor's approach.

1) Preprocessing Algorithm: The raw signal was expressed in sensor coordinates (s_s). As information in the body coordinate system was needed, the signal had to be converted from sensor to body coordinates (s_b). This was done using a rotation matrix (R_{bs}) (1), as previously proposed by Luinge *et al.* [18]. Briefly, the calibration procedure of the sternum sensor was as follows. First, the subject stood upright. During this, the body z-axis was equal to the gravity vector and could be expressed in the sensor coordinate system. Second, the trunk was bended forward around the hip-axis being the body y-axis, by which this axis could be expressed in the sensor coordinate system. The body y- and z-axis were cross-multiplied to obtain the x-axis. The bending task was repeated three times. The thigh and foot sensors were calibrated starting in a sitting posture. Subsequently, they were lifted while turning around the hip-axis (thigh) and knee-axis (foot). Finally, the arm was laid horizontally on a table and lifted while turning around the elbow-axis

$$\vec{s}_b = R_{bs}\vec{s}_s. \tag{1}$$

After this, the contents of the raw sensor signal were analyzed, namely, acceleration (a), gravity (g), offset (o), and noise (n) (2)

$$\vec{s}_b = \vec{a}_b - \vec{g}_b + o_b + n_b. \tag{2}$$

To obtain the acceleration signal, all other signal components were removed. First, a second-order low-pass Butterworth filter with a cut-off frequency of 23 Hz (H_{lpf1}) reduced high frequency noise (3)

$$\vec{s}_{b,1} = H_{lpf1}\left(\vec{s}_b\right) \approx \vec{a}_b - \vec{g}_b + o_b. \tag{3}$$

Assuming that there were no fast orientation changes of the sensor and, thus, no fast changes in the direction of gravity, gravity, and offset were estimated by low-pass filtering the signal. For this purpose, a second-order low-pass Butterworth filter having a cut-off frequency of 0.25 Hz (H_{lpf2}) was used. Subtracting this low-pass filtered signal from the original signal, which had already been compensated for high-frequency noise, provided the acceleration (4)

$$\vec{s}_{b,2} = \vec{s}_{b,1} - H_{lpf2}\left(\vec{s}_{b,1}\right) \approx \vec{a}_b. \tag{4}$$

The acceleration signal (a_b) was essential for further analysis. Furthermore, the low-pass filtered signal ($H_{lpf2}(s_{b,1})$) was useful for the estimation of body inclination. The inclination is defined as the angle of the body axes relative to the global vertical. As the direction of gravity equals the vertical axis in the global space, the orientation of the body relative to the global vertical is known when the gravity vector in the body system is known. Luinge *et al.* [19] showed that, although a better method exists, the low-pass filtered signal still gives a good estimate of the inclination. The average error of sensors placed on the trunk and pelvis was 3° with reference to an optical tracking system, with an increasing error with movement speed. Especially during slow movements, which are often present in PD, this method is useful. As calibrated signals were obtained from the Xsens software, the offset was negligible and therefore, the low-pass filtered signal was a good estimate of the inclination.

2) Activity Classifier: The AC uses the concept of a decision tree (see Fig. 3). The following features were used on the particular nodes. Node 1 used the Integrals of the Absolute value of the Accelerometer output (IAA, (5), [9]) to detect whether the person was performing a static or dynamic activity

$$\mathrm{IAA} = \frac{1}{t}\left(\int_0^t |a_x|\,dt + \int_0^t |a_y|\,dt + \int_0^t |a_z|\,dt\right). \tag{5}$$

The acceleration (a) of the thigh sensor was used in (5). As this feature sometimes missed slow movements (i.e., <0.25 Hz), which are especially present in PD patients, a second feature was introduced in this node. This feature identified the change in thigh inclination per second ($t = 1$ s), i.e., the difference in value of the inclination signal between one second and the next. When the difference was above a threshold, a dynamic activity was also recognized.

Node 2 was used to differentiate an upright trunk position from a horizontal one. This was accomplished by using the trunk sensor, assessing the inclination of the trunk [8]. The same principle was applied on node 4 using the thigh sensor, which distinguishes standing from sitting by assessing the thigh inclination. In node 6, active arm movement (AAM) was detected by determining the IAA of the acceleration measured in the wrist sensor.

The other branch of the tree considered the dynamic activities. Node 3 detected standing up, which was defined when the following sequence of events was recognized. First, the subject's thigh had to be orientated horizontally in global space.

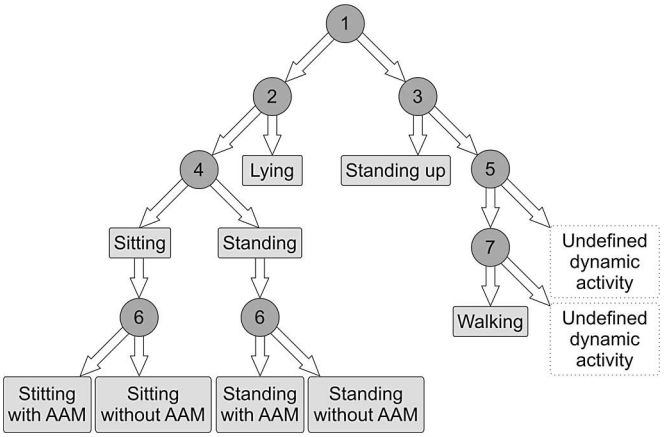

Fig. 3. Schematic overview of the decision tree for the classification of activities. The differentiation made in the binary decision nodes (BDN). BDN 1: Discrimination of static from dynamic activities. BDN 2: Discrimination of an upright from a lying posture. BDN 3: Discrimination of "sit to stand" from other possible motions. BDN 4: Discrimination of sitting from standing. BDN 5: Discrimination of dynamic activities in a standing posture from all other dynamic activities. BDN 6: Discrimination of postures with and without AAM. BDN 7: Discrimination of walking from all other "active standing" activities.

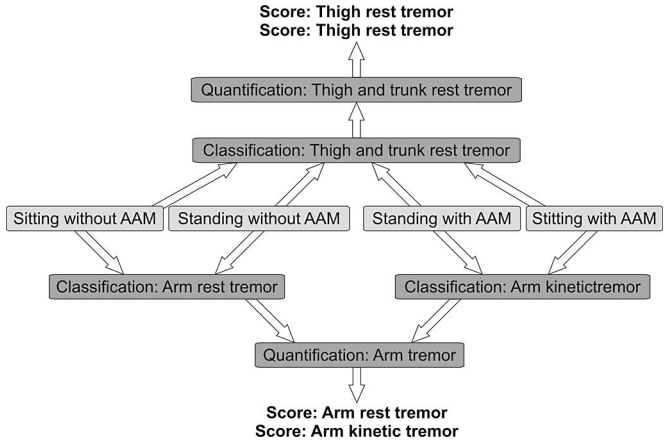

Fig. 4. Schematic overview of the detection and quantification of tremor. The middle boxes in light gray show the current activity. Dependent on the activity, different types of tremors are analyzed, resulting in scores for the different types of tremor.

Subsequently, an inclination change had to be present. For this purpose, a feature representing the change of inclination in the thigh over 1 s was used. During the inclination change, the orientation of the thigh had to be changed to a vertical one. A vertical orientation was defined using the same parameters as node 4. Finally, nodes 5 and 7 differentiated walking from other dynamic activities. Node 5 checked whether the orientations of the thigh and trunk were upright. Node 7 applied a method for walking detection based on, but not similar to, a method proposed by Najafi *et al.* [11]. First, a peak detection algorithm was applied on the acceleration signal measured on the foot, which was filtered below 5 Hz using a second-order Butterworth filter. Only sufficiently high peaks, thus, peaks above a certain threshold (determined during the algorithm's training procedure), were detected. Successive peaks with intervals of 0.25–2.25 s defined potential steps. Two successive potential steps defined walking.

3) Motor Symptom Monitor a) Tremor: Two types of tremor were evaluated, namely, rest and kinetic tremor. Arm rest tremor was only determined when the arm was not moving, thus, when the activities sitting or standing without AAM were identified by the AC (see Fig. 4). In contrast, arm kinetic tremor was only evaluated when sitting and standing with AAM were classified. Furthermore, thigh and trunk rest tremor were quantified during the entire sitting and standing time, i.e., sitting and standing with or without AAM (as the thigh and trunk were not moving during these activities).

For rest tremor evaluation, the acceleration was first filtered between 3.5 and 9 Hz [20] and subsequently windowed using a Blackman window. The window had a length of 3 s and it was shifted over the data each second. Subsequently, the frequency spectrum of each window was computed using fast Fourier transform. In the spectrum, the dominant frequency was determined. When the power of this frequency was sufficiently high, the tremor was identified. During the training of the algorithm, the threshold for tremor detection was determined per activity, i.e., sitting and standing without AAM, separately. Tremors detected in isolated windows were rejected. After this, the rms values (intensity) of the signal in all directions within the positively labeled windows were computed, as well as the percentage of time during which the tremor was present. The intensity (i) and the duration (d) of tremor together quantified tremor severity (TS) (6)

$$\mathrm{TS} = i\sqrt{d} \tag{6}$$

where TS was computed for all axes of the 3-D acceleration. The TS values of each axis separately, of each possible combination of two axes, and the three axes combined were computed. The combined axes were calculated using Pythagoras. This gave a total of seven different combinations of which the one that best quantified tremor was determined per body part. How well a parameter quantified tremor was tested by computing the correlation between the parameter and the UPDRS 20 scores.

A different method was used to evaluate kinetic tremor, because this type of tremor occurs during limb movement. This movement interferes with the previous tremor detection approach. First, a second-order Butterworth filter filtered the acceleration signal between 3.5 and 12 Hz [20]. Subsequently, the signal was windowed using 3-s Blackman windows, and slid over the data each second. For each window, the periodogram was computed. From the periodogram, the first- and second-order moment were calculated. Before the moments could be calculated, the total energy (E_x) of the signal had to be calculated using the Fourier transformed signal ($X(f)$) (7). The frequency (f) is normalized by the sample frequency

$$E_x = \int_{f=0}^{0.5} |X(f)|^2 \, df. \tag{7}$$

The total energy was subsequently used to normalize the moments. The first-order moment ($f_{m\,1}$) determined the mean

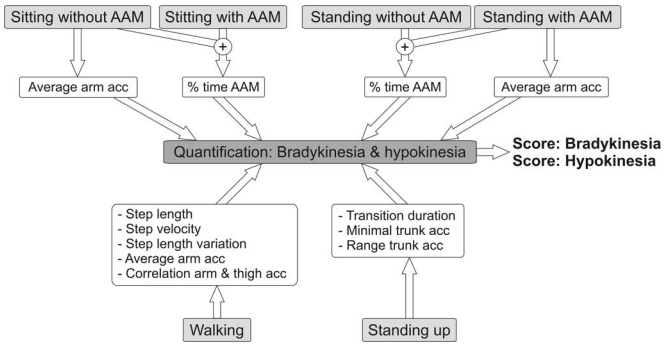

Fig. 5. Schematic overview of the quantification of bradykinesia and hypokinesia. The upper and lower boxes in light gray show the current activity. The white boxes represent the features that are extracted during these activities. Bradykinesia and hypokinesia are characterized using multiple parameters. The wide variety of parameters assessed provides a detailed analysis of bradykinesia and hypokinesia. acc = acceleration; corr = correlation.

frequency [21] (8)

$$f_{m1} = \frac{f_s}{E_x} \int_{f=0}^{0.5} f \left| X\left(f\right)\right|^2 df \tag{8}$$

where f_s represents the sample frequency. The second-order moment (f_{m2}) represents the variance in frequency, which provides a measure of spectral spread (standard deviation of the mean). This parameter is an indication of the bandwidth of the signal about the mean frequency. Equation (9) shows the computation of this parameter [21]

$$f_{m2} = \frac{f_s}{E_x} \int_{f=0}^{0.5} \left(f - f_{m1}\right)^2 \left| X\left(f\right)\right|^2 df. \tag{9}$$

The variance of the frequency was used to define whether the power was concentrated in a small frequency band around the mean frequency, which is the case for PD patients [22]. Kinetic tremor was detected when the value of the variance was beneath a certain threshold. The severity of the kinetic tremor was quantified by computing the percentage of time that kinetic tremor was observed. The amplitude was not used as a measure, because ordinary movement too heavily influenced this parameter. The variance of frequency (9), which is used to compute the percentage of time with kinetic tremor, is also influenced by ordinary movement, i.e., this parameter is increased by about 50% when ordinary movement is present in comparison to periods without movement. However, the average variance of frequency during periods of movement with tremor, i.e., 0.073 ± 0.027, still differs significantly from the value during periods of movement without tremor, i.e., 0.090 ± 0.031 ($P < 0.01$).

3) Motor Symptom Monitor b) Bradykinesia: Since bradykinesia manifests in many ways, several aspects of this phenomenon were assessed (see Fig. 5). The average value of acceleration represents the slowness of the movements. To obtain a meaningful parameter related to bradykinesia (and not hypokinesia), the average arm acceleration was only computed during periods with AAM. Because bradykinesia affects walking, parameters related to step length and step velocity were extracted during this activity. It had previously been demonstrated that the walking velocity decreases with a reducing step length [1]. Another feature of bradykinesia is the difficulty experienced during standing up [5]. Therefore, the duration of standing up and a range of movement parameters were extracted during this activity (see Fig. 5).

Step velocity and length were computed using an accelerometer and gyroscope placed on the foot. The validated algorithm proposed by Sabatini *et al.* [23] was applied for this purpose. Step length and velocity were normalized according to leg length. The length of the inside leg was measured manually using a ruler. Parameters related to standing up were extracted from the low-pass filtered trunk accelerometer signal using a second-order Butterworth filter with a cut-off frequency of 0.65 Hz [5]. This provided information about the inclination change in the upper body. From this signal, the transition duration was obtained by calculating the time between the two subsequent negative peaks [5]. The minimal trunk acceleration was defined by the peak with the highest negative value. Finally, the difference between the value of this same negative peak and the highest positive peak defined the range of trunk acceleration.

Finally, the average acceleration due to arm movement was computed during standing and/or sitting with AAM. This parameter was calculated by combining the 3-D acceleration using Pythagoras and subsequently taking the rms value. Previous to this, the acceleration was low-pass filtered below 3 Hz with a fourth-order Butterworth filter, to remove movement due to the tremor [20].

4) Motor Symptom Monitor c) Hypokinesia: Hypokinesia is characterized by the poverty of movement. This can be studied by assessing how much a patient moves his arms, which was defined by the time during which the arm was moving as a percentage of the entire sitting and/or standing time (see Fig. 5). The arm movement was studied after movement due to tremor was filtered off using the same procedure as applied in the bradykinesia evaluation. Hypokinesia also presents as diminished arm swing during walking [1]. In healthy people, the arm moves forward as the thigh moves backward and visa versa, which provides a high correlation between both in healthy people. However, when arm swing becomes random and there is a changing phase between arm and thigh swing, correlation decreases. As arm swing occurs slowly, it can be assessed by studying the acceleration signals below 1 Hz. Therefore, the correlation between the low-pass filtered ($<$1 Hz) acceleration signals of the arm and thigh were computed during walking. Furthermore, the amplitude of the arm swing diminishes in PD. For this reason, the average acceleration due to arm movement during walking was assessed.

C. Training the Algorithm

Training was performed to define the threshold values to be applied in the algorithm. These thresholds were needed for activity and tremor detection. During the training procedure, the activities determined by the algorithm while using different threshold levels, were compared to the activities defined by manual labeling of the video data. Manual labeling of the video data was performed per second during which both the current activity and the presence of tremor were determined.

The training was achieved using the leave-one-subject-out approach [24]. This method keeps training and test data strictly separated. The training set was created out of all subjects except one. This ''excluded" subject was used as the test set and was, thus, used to evaluate the performance of the PD monitor. This was repeated five times. During each time, the training set was composed of another combination of five subjects and the test set was composed of the ''excluded" subject. The results of subjects were combined to obtain the overall evaluation of the PD monitor.

D. Statistical Analysis

To assess the performance of the AC and tremor detection, the accuracy, the ability to correctly classify each window, was computed. Equation (10) shows the formulae used for the computation of accuracy, TP = true positives, TN = true negatives, FP = false positives, and FN = false negatives

$$\text{accuracy}(\%) = \frac{TP + TN}{TP + TN + FP + FN} \cdot 100 \qquad (10)$$

Furthermore, the PD monitor's ability to accurately score symptoms was assessed by comparing its output scores for the symptoms to the UPDRS scores given by the physician after analyzing the video data. This relation was quantified by the between-subject Spearman rank correlation. Finally, the use of the PD monitor to optimize treatment was assessed by analyzing its ability to discriminate different settings of the stimulator. This was assessed by a repeated measures ANOVA test and a subsequent Tukey test.

III. Results

A. Preprocessing

The inclination estimate was compared to the one of the Xsens softwares. They report a rms of 3°, while using the accelerometer, gyroscope, and magnetometer. We used the accelerometer only, to reduce the amount of sensors for future ambulatory use. Our estimation differed by 1.9° from the Xsens estimate.

B. Activity Classifier

The manually (video recordings) and automatically labeled activities were compared. Fig. 6 gives an example of one PD patient's trial. Table I gives the results of a test of the AC's ability to classify activities in PD patients. The AC achieved an overall accuracy of 98.9%.

Data of a healthy population were also used for training and evaluation of the AC. This gave slightly better results, namely, an overall accuracy of 99.3%. Especially, the activities walking and AAM during standing were detected better in healthy subjects.

C. Motor Symptom Monitor—Tremor

Rest tremor detection was performed with an accuracy of 84.5% during sitting and 94.1% during standing in the arm, while it was 79.1% during sitting and 90.1% during standing in the thigh. Kinetic tremor in the arm detection had an accuracy of 78.7% during sitting and 81.7% during standing.

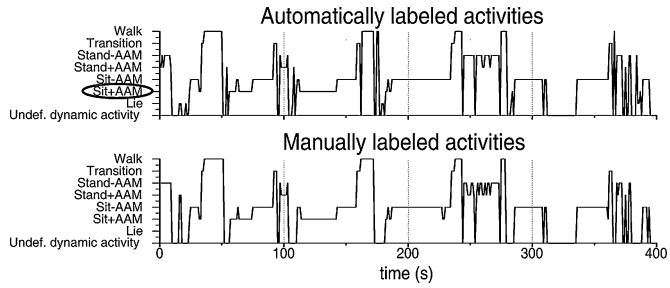

Fig. 6. Results of the AC. The figure shows manually and automatically labeled activities for one person during a 400 s during trial. The upper graph presents the activities labeled by the AC. The lower graph shows the manually labeled data using the video recordings. The manually labeled data act as a control for the automatic labeling of the AC. The activities determined by the AC show great similarity to the manually labeled data. During the encircled activity, sitting with AAM, the feature ''average arm acceleration" was computed (see Fig. 7).

TABLE I
EVALUATION OF AC–ACCURACY (IN PERCENT)

Activity	PD patients	Healthy control
Lie	99.6	100.0
Sit	99.3	99.7
Sit + AAM	98.9	99.4
Sit – AAM	98.7	99.3
Stand	99.1	99.9
Stand + AAM	98.6	99.7
Stand – AAM	98.9	99.5
Standing up	99.7	99.3
Walk	97.2	97.8
All	**98.9**	**99.3**

The evaluation of the AC for PD patients and healthy controls. The activities detected by the AC were compared to the activities manually labeled using the video data. The accuracy were determined per activity and an over all activities.

The ability of the MSM to quantify the various forms of tremor was assessed by comparing the output of the algorithm to the physician's UPDRS scores. For rest tremor in the arm, the best correlation between the PD monitor's output and the UPDRS scores was achieved when using acceleration data in the axial and radial direction while sitting, namely, a correlation of 0.84 ($P < 0.01$). A correlation analysis on rest tremor in the thigh was not performed, because too little variation in UPDRS scores given by the physician was present for a proper analysis. The correlation of the trunk rest tremor was also not computed, because it was not scored by the physician as it is not a standard UPDRS item. Quantification of kinetic tremor was assessed and proved to be more difficult, so a correlation of 0.67 ($P < 0.01$) to UPDRS item 21 was achieved during sitting. Furthermore, the severities of rest tremors, which were observed within one individual, were often different within the arm, thigh, and trunk. The same observation was made for rest and kinetic tremors, which also differed within individuals.

The ability of the MSM to discriminate between different settings of the stimulator was assessed by performing a repeated measures ANOVA test and subsequent Tukey test. Arm, thigh, and trunk rest tremor differed significantly between all conditions ($P < 0.05$, $P = 0.01$, and $P < 0.01$, respectively). Further-

TABLE II
EVALUATION OF AC–ACCURACY (IN PERCENT)

Activity	MSM-Parameter	Bradykinesia/ Hypokinesia	Correlation
Standing up	*duration*	B	0.70 ($P < 0.01$)
	minimal acceleration	B	-0.68 ($P < 0.01$)
	range of acceleration	B	-0.64 ($P < 0.01$)
Walking	*average arm movement*	H	-0.19 ($P = 0.47$)
	correlation thigh vs. arm movement	H	-0.43 ($P = 0.08$)
	step length	B	-0.70 ($P < 0.01$)
	step length variation	B	-0.03 ($P < 0.9$)
	step velocity	B	-0.71 ($P < 0.01$)
With AAM	*sit average arm movement*	B	-0.69 ($P < 0.01$)
	stand average arm movement	B	-0.72 ($P < 0.01$)
	sit & stand average arm movement	B	-0.57 ($P = 0.02$)
With & without AAM	*sit % of movement time*	H	-0.35 ($P = 0.17$)
	stand % of movement time	H	-0.24 ($P = 0.35$)
	sit & stand % of movement time	H	-0.48 ($P = 0.05$)

The evaluation of how well the MSM was able to score bradykinesia and hypokinesia. The values of bradykinesia and hypokinesia features were compared to the overall bradykinesia UPDRS score (UPDRS 31) given by the physician. The between-subject Spearman rank correlation between both values was computed. Correlations printed in black were significant, i.e. P - value < 0.05. Correlation printed in grey were not significant. B = Bradykinesia; H = Hypokinesia

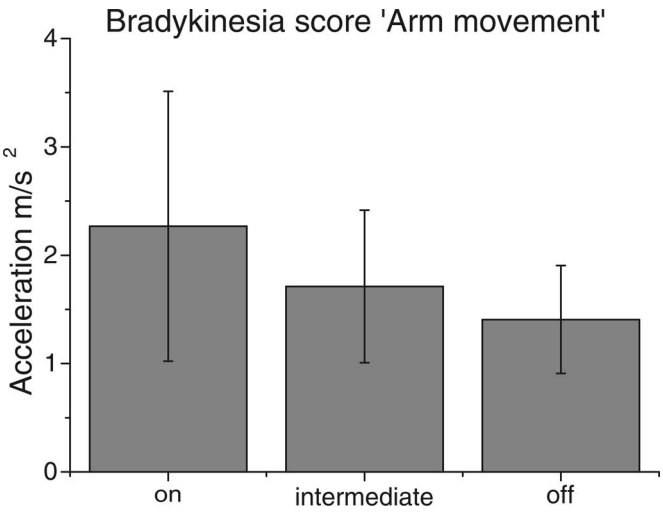

Fig. 7. Bradykinesia score ''average arm acceleration,'' which is determined during the activity sit with AAM (see encircled activity in Fig. 6), is compared per condition. The score is averaged over all subjects per condition, the mean, and the standard deviation of the mean are shown. A trend of a decrease in the average acceleration, representing worsening of bradykinesia, is shown as the treatment level is reduced.

more, the post-hoc Tukey test revealed significant differences between "on" and "off" (arm: $P < 0.05$, thigh $P < 0.05$, trunk $P < 0.01$) and between "intermediate" and "off" (arm: not significant, thigh: $P < 0.05$, trunk: $P < 0.05$). In contrast to rest tremor, no significant differences were found between severity levels of kinetic tremor during different stimulation settings. However, the trends were as expected. This means that kinetic tremor increased as the treatment level was reduced. An evaluation of the UPDRS test's ability to discriminate the conditions showed no significant differences (UPDRS item 20 arm: $P = 0.58$, thigh: $P = 0.70$, UPDRS item 21: $P = 0.77$).

D. Motor Symptom Monitor—Bradykinesia and Hypokinesia

The correlation between the output scores of the PD monitor for bradykinesia and hypokinesia and the UPDRS scores are summarized in Table II. As the parameters cannot directly be translated into single UPDRS items, we chose to compare them to item 31, which represents overall bradykinesia and hypokinesia. The table shows that most of the bradykinesia related parameters had a significant correlation with the UPDRS score. However, the achieved correlations were lower than those obtained for rest tremor. None of the hypokinesia-related parameters were significantly correlated with the UPDRS item 31. However, the hypokinesia parameter ''percentage of time during which the arm was active while standing and sitting'' just failed to reach significance ($P = 0.053$).

Bradykinesia and hypokinesia scores of the PD monitor did not differ significantly between the "off," "intermediate," and "on" states, although trends were as expected (i.e., less bradykinesia and hypokinesia in the "on" state). Fig. 7 shows an example of the bradykinesia score ''average arm movement during sitting'' averaged over all subjects per condition. This figure shows that bradykinesia worsens as the treatment level is reduced. Note that this trend is visible when averaging over all subjects, but individual patients may not always follow this trend. For example, one patient suffered from more severe bradykinesia during condition "intermediate" than during condition "off". The UPDRS item 31 scores did not show significant differences between conditions either ($P = 0.23$).

IV. DISCUSSION AND CONCLUSION

Currently, motor symptoms of PD patients are assessed by the use of short subjective tests performed in the hospital, such as the UPDRS. As this approach has some downsides, a new evaluation system would be beneficial. This paper presents a novel monitor to follow PD patients in their daily lives. Current objective PD monitors only assess general aspects of tremor, bradykinesia, and hypokinesia. The advanced PD monitor described in this paper assesses a wide range of aspects related to tremor, bradykinesia, and hypokinesia in order to gain a complete motor assessment of the patient. To accomplish this thorough analysis, an AC was incorporated into the PD monitor. Another advantage of the AC lies in the fact that it enables direct implementation of our PD monitor into an ambulatory environment. Although not further explored in this paper, the AC could eventually also be used to gain knowledge about the time spend on different activities during the entire day. The monitor uses a setup of four sensors worn on the thigh, wrist, and foot of the affected side and on the trunk. This was the minimal number of sensors required to accomplish the proposed analysis.

The inclination estimate and activity classification proved accurate. Subsequent tremor analysis comprised the evaluation of rest tremor in the arm, thigh, and trunk and the evaluation of kinetic tremor in the arm. The validity of the PD monitor in quantifying arm rest and kinetic tremor was demonstrated by the significantly high correlation with corresponding UPDRS scores. Differences between rest tremor in the arm, thigh, and

trunk as well as differences between rest and kinetic tremor within individual patients were observed. This underlines the importance of assessing different aspects of tremor, which is accomplished in our PD monitor.

The three aspects of bradykinesia and hypokinesia that were analyzed (arm movement, standing up, and walking) included features with a significant correlation to UPDRS item 31 score for overall bradykinesia and hypokinesia. However, whereas multiple bradykinesia parameters were correlated, none of the hypokinesia parameters were correlated. One reason for this might be that item 31 not solely quantifies hypokinesia, but also bradykinesia. This is an apparent advantage of our PD monitor, which makes a clear distinction between both symptoms.

After the accuracy of the motor symptom quantification was established, it was investigated whether the monitor could be used to optimize the treatment of PD. In the DBS patients, three conditions were analyzed: stimulator on, stimulator on with a stimulation amplitude at 80%, and stimulator off. The ability to distinguish the severity of tremor, bradykinesia, and hypokinesia at different DBS settings was evaluated. First, the PD monitor found the expected trends, i.e. the symptom worsened as the treatment level reduced. Second, it was shown that the values of rest tremor differed significantly between conditions. However, kinetic tremor, bradykinesia, and hypokinesia related parameters did not differ significantly between conditions. Still the results showed that the UPDRS test was not able to find any significant difference in symptoms severity between the conditions, whereas our PD monitor was. Therefore, our PD monitor proves to be a useful tool in optimizing treatment. Furthermore, the lack of significant differences can be explained by inter-individual differences in the severity of the disease, as well as differences in the response to DBS. The different responses to DBS are not only the result of differences in the way Parkinson is manifested in the patients, but may also be caused by inter-individual variations of the electrode position causing activation of different areas in the somatotopically organized subthalamic nucleus [25]. Therefore, the patients cannot be considered as a homogeneous group. This is also found in our results, as not all individual patients followed the expected trends of worsening symptoms with reducing treatment level. Finally, Krack *et al.* [26] argued that it could take several hours and even days before the effect of changes in DBS settings on bradykinesia stabilize. We chose to measure patients during a single day in order to circumvent day-to-day fluctuations. In addition, we limited our total measurement time to three hours, thereby avoiding fatigue in the PD patients. Therefore, our experiments started 15 to 30 minutes after adjustment of DBS, even though the effect of changing the settings on bradykinesia might not have been fully stable. This may have negatively influenced our results on bradykinesia evaluation.

Dyskinesia, which has been studied before by Keijsers *et al.* [27] and Hoff *et al.* [28], is not considered in this paper. Nonetheless, this is an important aspect that can be used to identify on and off-periods. Dyskinesia detection is also essential because bradykinesia cannot be quantified during a period of dyskinesia. For these reasons, the inclusion of dyskinesia detection in the PD monitor is an important next step in the development of the monitor. Another symptom not yet assessed by our monitor is freezing of gait, which would be classified as standing still by our current algorithm. We are currently performing studies to resolve this issue. A last topic not addressed in this paper, is the test-retest reliability. This is another essential next step before final implementation of the PD monitor.

In conclusion, this paper shows the PD monitor's accuracy in a thorough analysis of tremor, bradykinesia, and hypokinesia that can eventually be carried out in an ambulatory environment. Furthermore, it demonstrates that the monitor can be used to evaluate the PD motor symptoms in order to optimize treatment.

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