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EMG and Acceleration Signal Analysis for Quantifying the Effects of Medication in Parkinson's Disease

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Abstract— **Parkinson's disease (PD) is characterized by motor disabilities that can be alleviated reasonably with appropriate medication. However, there is a lack of objective methods for quantifying the efficacy of treatment in PD. We applied here an objective method for quantifying the effects of medication in PD using EMG and acceleration measurements and analysis. In the method, four signal features were calculated from the EMG and acceleration recordings of both sides of the body: the kurtosis and recurrence rate of EMG, and the amplitude and sample entropy of acceleration. Principal component approach was used for reducing the number of variables. EMG and acceleration data measured from nine PD patients were used for analysis. The patients were measured in four different medication conditions: with medication off, and two and three and four hours after taking the medication. The results showed that in eight patients the EMG recordings changed into less spiky and the acceleration recordings into more complex after taking the medication. A reverse phenomenon in the signal characteristics was observed in seven patients 3-4 hours after taking the medication. The results indicate that the presented method is potentially useful for quantifying objectively the effects of medication on the neuromuscular function in PD.**

I. INTRODUCTION

In Parkinson's disease (PD) there is a dopaminergic neuronal loss in the substantia nigra in the brain, which leads to four primary symptoms of PD: resting tremor, rigidity, bradykinesia and postural instability [1]. Although there is no cure for PD, the symptoms can be alleviated reasonably with medication that aims to dopamine replacement in the brain [2]. However, there are no objective methods in clinical use for quantifying the efficacy of treatment in PD. The disability and impairment in PD are most commonly evaluated subjectively by using standardized rating scales such as the Unified Parkinson's Disease Rating Scale (UPDRS) [3]. Therefore, there is a need for objectively measured and quantified PD characteristics for improving the diagnosis, for quantifying treatment efficacy and for monitoring disease progression [4].

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Surface electromyography (EMG) and kinematic measurements can be used for objectively quantifying neuromuscular function and movement. These measurements may therefore be useful for quantifying the effects of treatment in PD. Previous studies have found that the antiparkinsonian medication may change the EMG spectrum [5], [6] and the tremor-EMG coherence [6]. In addition, it may change the EMG burst characteristics and the movement speed during rapid point-to-point movements of limbs [7], [8]. Medication may change the amplitude and the regularity of tremor as well [5], [6]. The previous studies have analyzed differences in the signal characteristics between medication on- and off-states. However, the understanding about the neuromuscular disorder in PD could be increased by analyzing the signal characteristics as a function of time before and after taking the medication.

We apply here an objective method for quantifying the effects of medication in PD using EMG and acceleration analysis and test the method with the measured data. Eight parameters capturing PD characteristic signal features were first extracted from the EMG and acceleration recordings of nine PD patients. These signal features were selected for analysis based on their previous usability in discriminating between PD patients and healthy persons [9], [10]. Principal component (PC) approach was used for reducing the number of variables. Finally, the effects of medication were quantified by examining the first PCs in four different medication conditions (with medication off and 2-4 hours after taking the medication). The hypothesis of this study was that the used method is capable of detecting objectively medication induced changes in the neuromuscular and motor function of PD patients.

II. METHODS

A. Measurements

Nine PD patients participated in this study after giving their informed consent. The clinical characteristics of the patients are presented in Table I. This study was approved by the Local Human Ethics Committee of the Kuopio University Hospital. The measurements were performed four times for each patient: 1) with medication off (no medication 24 hours prior to the measurements), 2) two hours after taking the medication, 3) three hours after taking the medication and 4) four hours after taking the medication. The medications were individual and they are detailed for each patient in Table I. The UPDRS -motor scores were assessed for each patient prior to each measurement.

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TABLE I

CLINICAL CHARACTERISTICS OF PATIENTS

Patient no.	Age	Gender	UPDRS off	Medications
1	73	F	23	Madopar 100 mg/25 mg 1x3, Eldepryl 10 mg 1x1
2	57	M	67	Eldepryl 5 mg, Stalevo 50 mg 1x6, Sifrol 0.7 mg 1.5x3 (Sinemet 0.5x50 mg)
3	75	M	28	Sinemet depot 1x3, Sifrol 0.7 mg 1x3
4	68	M	18	Sifrol 0.7 mg 1.5x3, Eldepryl 10 mg
5	78	M	26	Sifrol 0.7 mg 1x3, Eldepryl 1x1, Ipsatol 1.5x3
6	55	M	69	Madopar 100 mg/25 mg, Sifrol 0.7 mg 0.5x3, Eldepryl 5 mg 1x1
7	75	M	58	Sifrol 0.7 mg 1.5x3, Stalevo
8	57	M	48	Sifrol 0.7 mg 1x3, Stalevo 100 mg/25 mg/200 mg, Efexor depot 75 mg 1x1
9	58	M	31	Eldepryl 10 mg 1x1, Sifrol 0.7 mg 1.5x3

UPDRS off means the total UPDRS -motor score with medication off

During the measurements, the subjects were asked to hold their elbows at 90° angle with their palms up for 30 seconds. No additional weights were used. Bipolar surface EMGs were registered continuously from the biceps brachii (BB) muscles and the tri-axial accelerations of forearms simultaneously from the wrists. The measurements were done by using ME6000 -biosignal monitor (Mega Electronics Ltd., Kuopio, Finland), disposable Ag/AgCl electrodes (Medicotest, model M-00-S, Ølstykke, Denmark) and accelerometers (Mega Electronics Ltd., range $\pm$ 10 g, 14-bit AD converter). The recording electrodes were placed bilaterally over the BB muscles with 3 cm interelectrode spacing and reference electrodes laterally 6-7 cm from the recording electrodes. The sampling rate was 1000 Hz.

B. Signal analysis

EMG and acceleration signals were pre-processed as follows. First, 10 seconds long segments of EMG and acceleration were chosen from the middle of the isometric contraction for analysis. The total acceleration was calculated as a resultant of the three acceleration components. Then, the low-frequency trends (mainly movement artifacts) were removed from both signals by using a smoothness priors method [11]. The high-pass cutoff frequencies were 10 Hz for EMG and 2 Hz for acceleration.

We calculated four signal features from the EMG and acceleration recordings of both sides of the body (resulting in eight features): 1) kurtosis of EMG (k), 2) recurrence rate of EMG ($\%\mathrm{REC}$), 3) RMS amplitude of acceleration (RMS) and 4) sample entropy of acceleration (SampEn). The signals were divided into overlapping epochs (epoch length 2048 ms, overlap 75 %) and all parameters were calculated for the overlapping epochs and finally averaged over the epochs as in [9], [10].

We calculated the kurtosis of EMG, which is the fourth centered moment of a time series x

$$k = \frac{E\{(x-\mu)^4\}}{\sigma^4}, \tag{1}$$

where μ is the mean of the sample values and σ the standard deviation. Kurtosis is higher for more spiky signals and it was higher for PD patients than for healthy controls in [10]. We calculated two parameters of nonlinear dynamics as described in [12], [13]: the recurrence rate of EMG and the sample entropy of acceleration. $\%\mathrm{REC}$ measured the percentage of recurring structures in the EMG signal. In previous studies [9], [10], it was higher for PD patients than for healthy persons. The sample entropy described the complexity of the acceleration resultant. It measured the negative natural logarithm of the conditional probability that two segments in the signal that were similar for m points ($m = 2$) were also similar for $m + 1$ points. In [9], it was lower for PD patients than for healthy persons.

We used a principal component approach [14] for reducing the number of variables and for transforming the original possibly correlated variables into uncorrelated variables. The calculated PCs worked better in following the effects of medication than the single EMG and acceleration parameters. In that approach, the calculated parameters (that were normalized to zero mean and unit SD) were used to form high-dimensional feature vectors z.

$$z = [k_r \;\; k_l \;\; \%\mathrm{REC_r} \;\; \%\mathrm{REC_l} \;\; \mathrm{RMS_r} \;\; \mathrm{RMS_l} \ldots \\ \mathrm{SampEn_r} \;\; \mathrm{SampEn_l}]^{\mathrm{T}}, \tag{2}$$

where the subscripts r and l denote the right or the left side of the body. Four feature vectors were formed per each patient. Each feature vector corresponded to one medication condition of one patient.

The dimension of the feature vectors was then reduced by using the PC approach as described in [9]. Briefly, the feature vectors were decomposed into weighted sums of basis vectors where the scalar weights are called the PCs. The basis vectors were chosen as the eigenvectors from the correlation matrix of the feature matrix (that contained the feature vectors of all subjects). Four eigenvectors corresponding to the four largest eigenvalues were chosen as the basis vectors. They contributed to 95 % of the total variation in the feature vectors of all subjects. The first eigenvector was the best mean square fit for the feature vectors of all subjects. Therefore, the first PC (PC1) described the amplitude of the original signal parameters with respect to the mean of all subjects. PC1's contribution was 71 % of the total variation and it worked best in diffentiating between different medication states. The addition of other PCs into the analysis

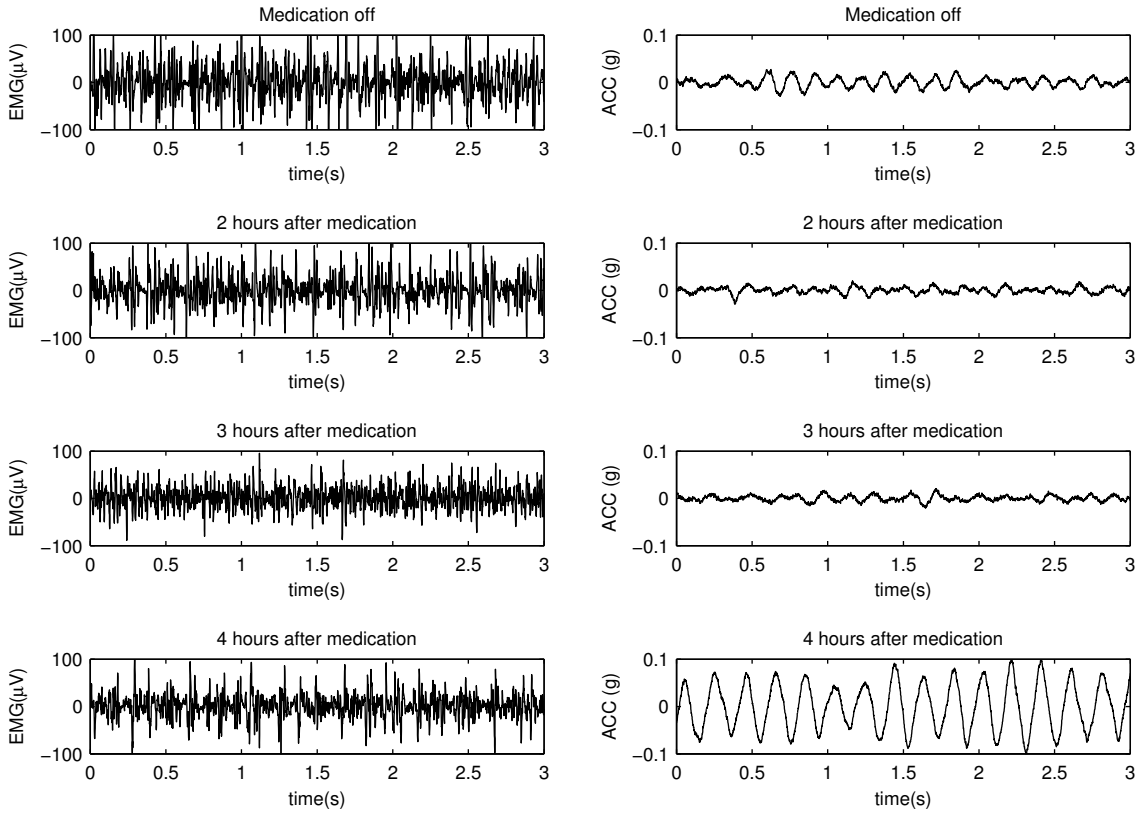

Fig. 1. EMG and acceleration measurements of Patient no. 6 with medication off and with 2 - 4 hours after taking the medication.

did not increase the discriminating power. Therefore, PC1 was chosen for deeper analysis.

III. RESULTS

The EMG and acceleration measurements of one PD patient (Patient no. 6, right hand) in each medication condition (with medication off and 2 - 4 hours after taking the medication) are presented in Fig. 1. One can observe differences in the measurements between different medication conditions. The amount of spiky and recurring EMG structures and the amplitude of acceleration (tremor) decrease after taking the medication and start to increase 3-4 hours after taking the medication.

The calculated PC1s and the total UPDRS -motor scores in each medication condition for all patients are presented in Fig. 2. In addition, the first eigenvector is presented in the same figure. One can observe that the total UPDRS -motor scores decrease after taking the medication for all patients. This means that the severity of motor disorders reduces with medication for all patients. Correspondingly, the PC1 values decrease after taking the medication for all other patients than Patient no. 8. By examining the first eigenvector in Fig. 2 one can conclude that the reduction in PC1 values indicates that the EMG measurements get less spiky (lower k) and they contain less recurring structures (lower $\%\mathrm{REC}$). In addition, it indicates that the amplitude of acceleration decreases (lower RMS) and the complexity of acceleration increases (higher SampEn) with medication.

One can observe in Fig. 2 that the severity of motor disorders starts to increase 2 - 3 hours after taking the medication for all patients. The increase in the clinical UPDRS -scores indicates that the efficacy of medication starts to weaken some time after taking the medication. Correspondingly, the PC1 values start to increase 2 -3 hours after taking the medication for all other patients than Patient no. 7 and Patient no. 8. The increase in the PC1 values and in the total UPDRS motor scores does not happen at the same time for all patients, which indicates that these scores (PC1 and UPDRS) do not measure exactly the same thing.

IV. CONCLUSIONS

Currently, there is a lack of objective methods for quantifying the efficacy of treatment in PD. We used here an objective method for quantifying the effects of medication on PD patients by using EMG and acceleration measurements and analysis. The results showed that by using the presented method we could detect similar medication induced changes in the signal characteristics of eight out of nine patients after taking the medication and a reverse change in seven patients 3-4 hours after taking the medication. It must be noted that these patient measurements were made during years 2006 - 2007 and there has been development in the antiparkinsonian medications since. The results indicate, however, that the presented method is potentially useful for quantifying objectively the effects

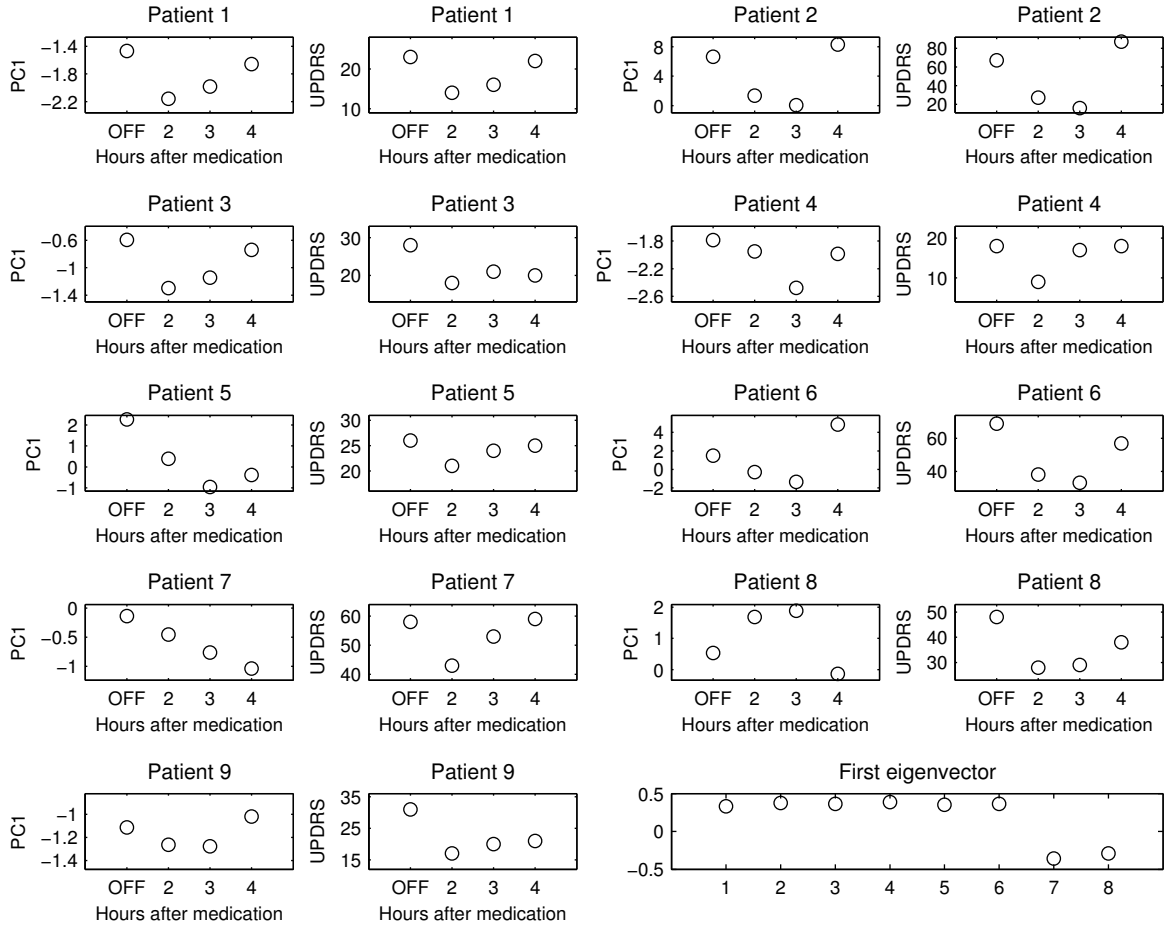

Fig. 2. The first principal components and the total UPDRS motor scores with medication off and with 2 - 4 hours after taking the medication. The first eigenvector (bottom right) that corresponds to the feature vector in Eq. (2).

of medication on the neuromuscular and motor function of PD patients. Further studies are suggested for quantifying the sensitivity of the method to different types of PD and for quantifying the stability of the measures over time with control data.

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