Evaluation of Parkinson's Disease at Home

Evaluation of Parkinson's Disease at Home: Predicting Tremor from Wearable Sensors

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***Abstract*— The continuous monitoring of Parkinsons's disease (PD) symptoms would allow to automatically adjust medication or deep brain stimulation parameters to a patient's momentary condition. Wearable sensors have been proposed to monitor PD symptoms and have been validated in a number of lab and hospital settings. However, taking these sensors into the daily life of patients introduces a number of difficulties, most notably the absence of an observable ground truth of what the user is currently doing.**

In this pilot study, we investigate PD symptoms by combining wearable sensors on both wrist and the chest with a questionnaire based evaluation of PD symptoms, in the form of experience sampling method. For a tremor dominant patient, we show that experienced tremor severity can be predicted from the sensor data with correlations of up to $r = 0.43$. We evaluated different window lengths to calculate the features in and see better results for longer window lengths. Our results show that continuous monitoring of PD symptoms in daily life is feasible using wearable sensors.

I. INTRODUCTION

Parkinson's disease (PD) is a degenerative disorder in which a loss of dopaminergic neurons in the substantia nigra causes motor and non-motor symptoms. Cardinal motor symptoms are bradykinesia, rigidity, tremor and postural instability. The vast majority of PD patients is treated with dopaminergic medication, e.g. levodopa, to restore dopamine levels in the basal ganglia. A well-known challenge of this pharmacological treatment is the occurrence of intra-daily motor fluctuations and levodopa-induced dyskinesia after five to ten years [1]. These fluctuations are also known as ON- and OFF-fluctuations, where ON-state refers to periods during which motor symptoms are well treated, and OFF-state refers to periods during which motor symptoms are not treated sufficiently. Suffering from ON-OFF fluctuations can be an indication for deep brain stimulation (DBS), which then aims to increase the time a patient spends in ON-state. Therefore, monitoring these intra-daily fluctuations is of importance to control and adjust dopaminergic restoration therapy, and maybe even DBS in the future [2].

Wearable sensors, in particular inertial measuring units consisting of accelerometers and/or gyroscopes, have potential to monitor PD symptoms and ON-OFF fluctuations in a continuous, non-obtrusive manner. Further validation of systems and preferably care-models is needed before they are applicable for daily life monitoring [3], [4]. Studies monitoring tremor during daily life activities are often limited because data were collected in simulated home settings in either a research lab or hospital [5], [6], [7], [8], [9]. Although the real-life representation of a simulated home setting stays debatable, videotape recordings of the assessments can be made and be used as parallel 'ground truth' data. Studies which are performed in the real home situation are however limited because of the lack of such parallel ground truth data [3]. This highlights one of the major challenges in PD monitoring; the availability of reliable ground truth data on the patients clinical state.

We introduce experience sampling method (ESM), also known as ecological momentary assessment, to provide additional subjective data on the patient's well-being to verify and evaluate our wearable sensor data [10]. The smartphone-based ESM method we used, presents digital questionnaires at semi-randomized moments throughout the day asking the patient about current motor state and symptoms. Additionally, there are accompanying questions on mood, affect and context, which can also fluctuate and cannot be measured directly from the wearable sensors.

The development and validation of the ESM-method will be described elsewhere. In this case report, we describe a tremor-dominant PD patient who reported to suffer from ON-OFF fluctuations. We demonstrate how fluctuations in tremor severity, measured by ESM, can be predicted from wearable sensors during daily living.

II. MATERIAL AND METHODS

A. Study Design

During a period of two consecutive weeks, participants had to wear three wearable sensors (one at each wrist and one at the chest) and had to complete ESM questionnaires.

1) Wearables: This study used MOX5 wearables (Maastricht Instruments, Maastricht, The Netherlands), containing both an accelerometer and gyroscope. The accelerometer covered an amplitude range of ± 8 g and the gyroscope covered a range of ± 2000 deg/s. Data were collected with a sampling rate of 200 Hz. The wearables were attached to the body via handmade wristbands and a necklace (Fig. 1). Participants had to wear the wearables only during daytime, and had to charge them at night. For subsequent alignment to the ESM questionnaires, the data were time stamped on the devices. Data were saved on the device and were extracted by the research team after the measurement period.

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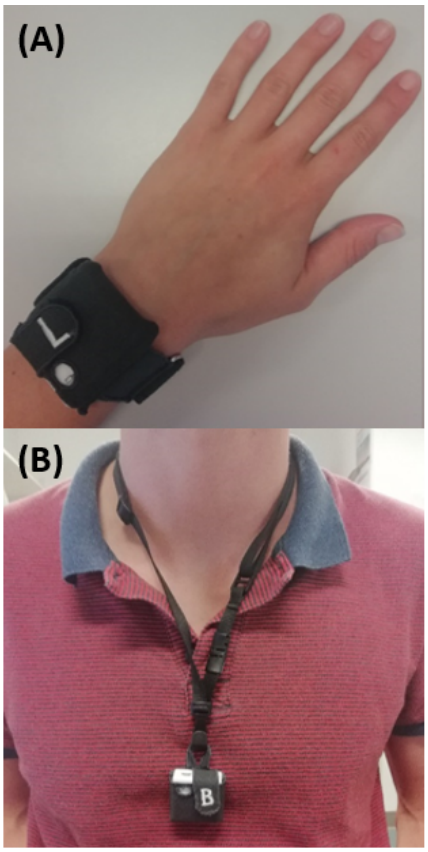

Fig. 1. Wrist-worn (A) and chest (B) sensors including accelerometer and gyroscope as well as flash storage and batteries. Participants wear the sensors from waking up until they go to bed and charge them during the night.

2) ESM: The ESM app Psymate[1] was installed on the participants smartphone. We developed a specific PD questionnaire using previous work [11], [12] and by patient and clinician interviews about what is considered important when identifying inter- and intra-daily fluctuations in PD symptoms. During the measurement period, participants received repetitive questionnaires (containing 26 questions) at seven semi-randomized moments during the day. These questionnaires contained questions on mood, affect, context, motor state and PD symptoms at that specific moment (e.g. I experience tremor). Participants had to rate the questions on a 7-point Likert scale. The questionnaires stayed available for only 15 minutes, thereby excluding recall bias. The participants were asked to complete as much questionnaires as possible without adapting their normal daily behaviour.

B. Participants

This study was approved by the METC azM/UM and written informed consent was obtained from all participants. Recruitment was done by neurologists, neurosurgeons, and PD nurses at the Maastricht University Medical Centre. Inclusion criteria were: Diagnosed with idiopathic PD; in possession of a smartphone (iOS or android); mastering Dutch language; and being available for two consecutive weeks of representative daily activities. Patients were excluded if they scored less than 24 points on the Montreal Cognitive Assessment [13]. We included and finished data collection in 20 participants.

To be sure to have sufficient fluctuations in tremor severity for this pilot study, we investigate the case of a participant that reported to be tremor dominant and to suffer from severe ON-OFF fluctuations. This participant is a 65-year old male who has been diagnosed with idiopathic PD for 6 years. He scored 26 points on the Montreal Cognitive Assessment. Since one year this participant receives bilateral subthalamic DBS therapy. In addition to the DBS therapy, he takes dopaminergic medication five times a day (levodopa equivalent daily dose = 788). The patient reported ON-OFF fluctuations which were medication related, resulting in periods of increased tremor ranging from approximately half an hour before standard medication intake moments until a quarter after medication intake.

C. Data Processing

In order to align the continuous sensor data to the relevant subjective evaluations measured through ESM, we extracted the 15 minutes of sensor data prior to each completed questionnaire. We hypothesize that the previous 15 minutes best reflect the participants symptomatic experience. Each of these 15 minute long blocks is then associated with the corresponding answers from the ESM questionnaire. To extract meaningful information from the sensor data, we extracted features both in the time and spectral domain [14]. We evaluate different window lengths for the feature extraction. Fig. 2 visualizes our feature extraction procedure.

D. Feature Extraction

Based on previous work [5], [9], [15] in the detection and decoding of tremor and bradykinesia in lab or hospital settings, we extracted the following features:

1) Logarithmic signal energy in the 3.5-7.5 Hz frequency band. We extracted this information from both accelerometer and gyroscope data. (6 features)
2) Total signal energy in the form of the root mean squared signal. This feature was extracted from the low-pass filtered (3 Hz) accelerometer data. (3 features)
3) The dominant frequency in the low-pass filtered (3 Hz) accelerometer data. (3 features)
4) The dominant energy ratio, which we calculated by dividing the maximum energy by the total energy in the low-pass filtered (3 Hz) accelerometer data. (3 features)
5) The amplitude range, which we extracted from the low-pass filtered (3 Hz) time series of accelerometer data. (3 features)
6) Maximum normalized cross-correlation and corresponding temporal offset among all pairs of low-pass filtered accelerometer time-series data. (2 features)

[1]http://www.psymate.eu

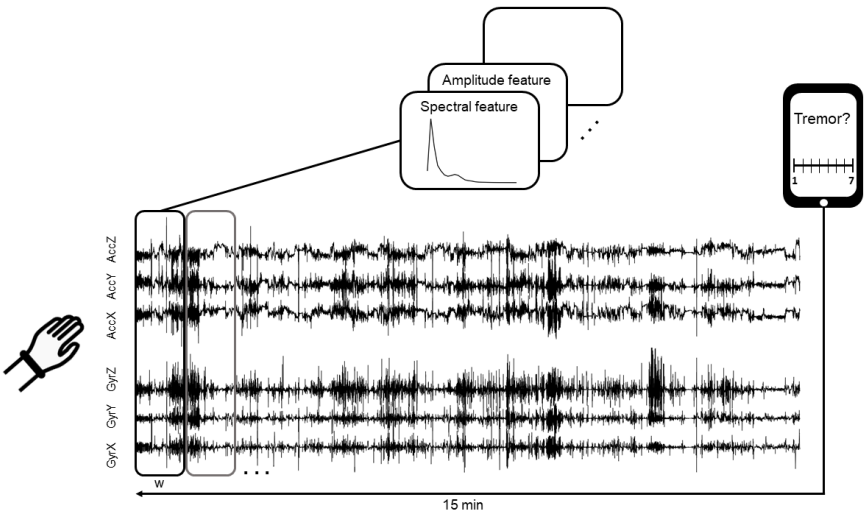

Fig. 2. Feature extraction procedure. For each ESM questionnaire, we extract the proceeding 15 minutes of continuous sensor data. We divide these into windows of varying length w and extract different features. The extracted feature vectors are then annotated with the answers from the corresponding questionnaire.

This results in a total of 20 features for each of the three wearables and thus a total of 60 features. To investigate the effect of window length and see which window length best represents the patient's answers, we extracted these features in non-overlapping windows of 30, 60, 120, 180, 300 and 900 seconds. We assigned the same answers from the corresponding questionnaire to all windows extracted from one block of sensor data. Please note that this leads to different amounts of samples for the different window length conditions. While the 900 second long windows result in 62 samples (= number of filled-out questionnaires), the 30 second long windows result in $62 \cdot 30 = 1860$ samples. This also results in vastly different baseline levels, which we estimate using permutation levels (see Section II-E).

E. Data Analysis

For this pilot study, we focused on both wrist worn sensors and excluded the chest sensor. This results in a total feature space of 40. To test the prediction of tremor severity from the extracted features, we applied a 10-fold cross-validation. In this approach, 90% of the data are used for training and the remaining 10% are used for testing, this is repeated until all samples have been used for testing exactly once. To predict the continuous severity assessments, we employed a simple linear regression. We calculated Pearson correlations between original and predicted tremor severity to evaluate the prediction.

We tested statistical significance through random permutation tests, in which we randomly shuffled the severity scores and calculated correlations between original and shuffled scores. This process was repeated 1000 times and the 95% highest correlations were used as a random baseline to signify the $\alpha = 0.05$-level.

III. RESULTS

Correlation coefficients between original and predicted tremor scores are significantly above chance level for all window lengths except for the 120 second long windows (Fig. 3 (A)). This drop is further characterized by higher correlation coefficients for shorter (above 0.15 for both 30 and 60 seconds) and longer windows (180 seconds and above). Highest correlation scores were obtained for 15 minute long windows with $r = 0.43$. Fig. 3 (B) shows an example of predicted and actual tremor scores for 15 minute long windows.

IV. DISCUSSION

The evaluation of PD symptoms in continuous monitoring during daily life activities is very challenging, as no ground truth is available. Patients might sit still in front of the TV, be engaged in a conversation or take a walk in the park. These different activities will have tremendous effects on the measured sensor data and variations need to be taken into account before reliable prediction of symptoms can be achieved. Our preliminary results give compelling evidence that features that are known to be successful in the prediction of PD symptoms in lab settings [15], can be used to predict tremor severity during the patients daily life. These results expand previous work which did make use of activity detection using videotapes, clinical assessments, and predefined motor tasks [5], [6], [7], [8], [9]. In addition, our results expand previous work which predicted clinical tremor scores from tremor data which was recorded while patients were comfortably seated in a chair [16]. Lastly, this study is to our knowledge the first one comparing the effect of using different window lengths for tremor feature extraction. Longer window lengths resulted in better correlation results of the predicted ESM scores. It is important to note that the chance level results are also higher for longer windows, as

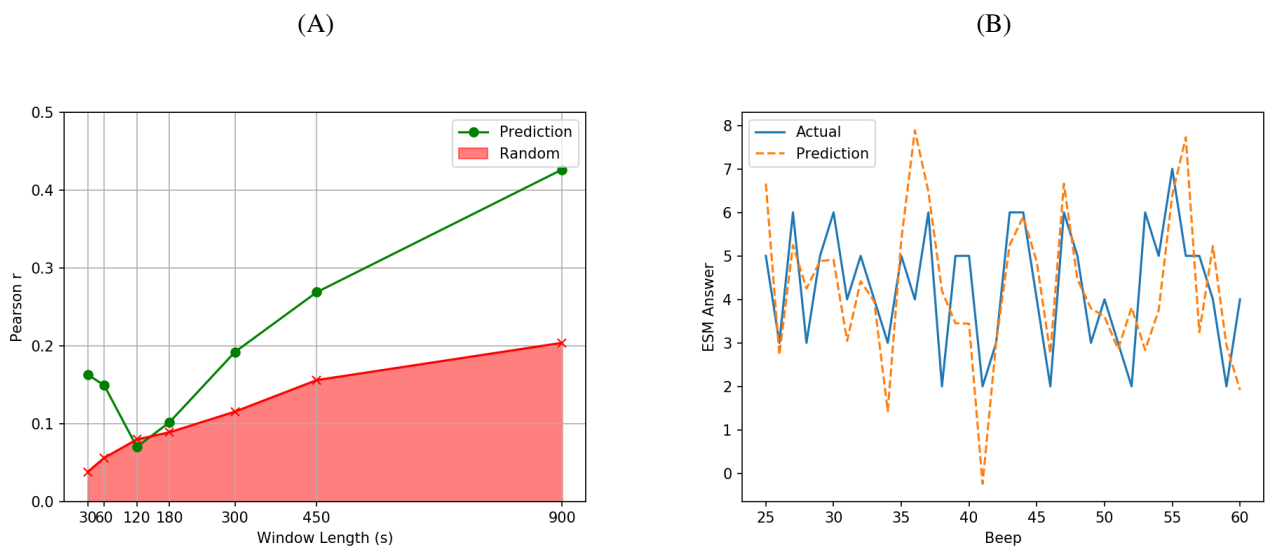

Fig. 3. Mean correlation results for tremor severity (A). Correlation coefficients for all but the 120 second window length are significantly above chance level (red shaded area, $\alpha = 0.05$). Example of actual (blue) and predicted (yellow) tremor scores for the full 15 minute window condition (B).

the number of samples decreases and high correlations are more likely in smaller sample sizes.

Clearly, our results need to be extended to more patients with different amounts of ON-OFF fluctuations and to other PD motor symptoms, such as bradykinesia, rigidity, and dyskinesia.

V. CONCLUSION

In this case report, investigating fluctuating PD tremor in a patient's daily life, we show that subjective tremor scores can be predicted with good correlations from wrist-worn sensors using very simple regression models. We employ standard features from the literature and investigate the influence of different window lengths on the prediction quality. For analyses of this individual patient, longer window lengths seem to result in better prediction quality. This confirms the possibility of, and increases the knowledge on monitoring PD symptoms in a daily life situation.

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