A Wearable Automated System to Quantify Parkinsonian Symptoms Enabling Closed Loop Deep Brain Stimulation

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Abstract. This study presents (1) the design and validation of a wearable sensor suite for the unobtrusive capture of heterogeneous signals indicative of the primary symptoms of Parkinson's disease; tremor, bradykinesia and muscle rigidity in upper extremity movement and (2) a model to characterise these signals as they relate to the symptom severity as addressed by the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS).

The sensor suite and detection algorithms managed to distinguish between the non-mimicked and mimicked MDS-UPDRS tests on healthy subjects ($p \leq 0.15$), for all the primary symptoms of Parkinson's disease. Future trials will be conducted on Parkinsonian subjects receiving deep brain stimulation (DBS) therapy. Quantifying symptom severity and correlating severity ratings with DBS treatment will be an important step to fully automate DBS therapy.

Keywords: Parkinson's disease therapy device · Quantification of Parkinson's disease symptoms · Rigidity model

1 Introduction

Parkinson's disease (PD) is a progressive disease that presents the gradual loss of both motor and non-motor functions. The primary motor symptoms of Parkinson's disease have been the main topics of research for a considerable amount of time and consist of tremor, bradykinesia and muscle rigidity. There is currently no cure but treatment can be administered in the form of oral medication or deep brain stimulation (DBS) during therapy sessions. The Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) is an internationally recognised scale used by clinicians to evaluate and monitor PD-related disabilities and impairment through interview and observation. Part III of the MDS-UPDRS evaluates and scores the severity of the primary motor symptoms of the patient.

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To the author's knowledge, there has been no attempt to correlate quantifiable data of primary symptoms to these DBS parameters, i.e. automating DBS therapy. The sensor suite described in this study will look to eventually correlate the symptom severity to DBS parameters. As an initial step, this study focuses on the validation of the sensor suite on healthy subjects.

The system also has the potential to be used in conjunction with Parkinson's disease rehabilitation robots. By providing an objective and quantifiable rating for each symptom, the robot can then conduct an improved and custom procedure for more efficient rehabilitation.

The proposed experiment in this study will be conducted on healthy subjects who will undergo symptom severity tests without mimicked symptoms and with mimicked symptoms of Parkinson's disease. The objectives of this experiment are to record baseline results, from the non-mimicked tests, with the sensor suite (MDS-UPDRS = 0) for comparison purposes in future trials with Parkinson's subjects, and to determine specific models for quantifying primary symptoms of Parkinson's disease.

Rigidity is defined as increased muscle tone which is felt as resistance to passive movement. Mechanical impedance and viscoelastic properties (VEPs) of the affected limbs have been used in literature in an attempt to measure rigidity [1–4]. Mechanical impedance is defined as the vectorial sum of the viscous and elastic stiffness. VEPs are defined as the viscous stiffness and elastic stiffness. Impedance and VEPs metrics will be explored and compared in this study.

Bradykinesia restricts the speed of movement of limbs such as the rotation of the wrist. A gyroscopic sensor attached to a subject's forearm can be used to measure the rotational speed of the wrist [5,6]. Bradykinesia in theses studies was quantified using three parameters; the average angular velocity, the percentage of time the hand was active in a particular time window and the average range of rotation of the hand. Average angular velocity performed best in distinguishing the presence of bradykinesia and will therefore be utilised in identifying bradykinesia for this study.

The involuntary shaking experienced by a patient can be defined as tremor. Tremor has attempted to be quantified in PD patients using IMUs [7,8] to measure the accelerations of the affected limb. A predicted MDS-UPDRS tremor score was produced from linear regression of the peak powers of the accelerometers and gyroscopes. Peak power analysis of acceleration measurements will also be explored in the current study to identify tremor.

2 Methods

2.1 Recording Devices

A 6-axis force/torque transducer from ATI Industrial Automation was utilised for this experiment. The force transducer was attached to the wrist because it is the area of the forearm with least muscle mass and therefore least compliance. A joystick-like handle was attached to the force transducer to allow better control for the clinician of the subject's forearm during rigidity assessments. The force

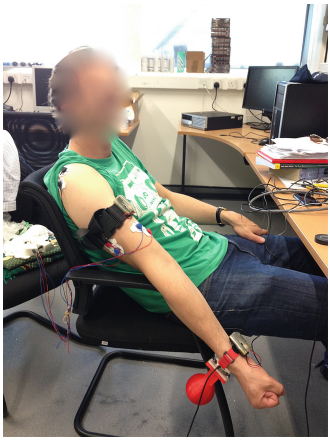

Fig. 1. The device setup on a healthy subject

transducer was only used during the rigidity assessments. All forces and torques during the experiments were sampled at 1 kHz.

Inertial measurements units (IMUs) from x-io were attached to the forearm and upper arm to areas with the least muscle mass to minimise compliance. The IMUs included an accelerometer, a gyroscope and a magnetometer. IMU data were sampled at 64 Hz.

The data from all sensors were streamed to a laptop running a GUI program that displayed and recorded the data. A set-up on a subject is shown in Fig. 1. All data outputted from the sensors were validated before use in clinic.

2.2 Subjects

Four (three male, one female) healthy volunteers participated in the study. The mean age of the volunteers is 20 years old. The control subjects were neurologically and physically healthy. All subjects gave informed consent under the Ethics agreement of the Imperial College Research Ethics Committee.

2.3 Testing Protocol

Each subject was asked to sit on a chair with both arms rested. All sensors were then attached to the subject's arm and connected to the laptop for data collection. The testing process was verbally explained and physically demonstrated to each subject before tests began. The total time required from each subject, with 1 min rests between assessments, did not exceed 30 min. Each of the assessments described below are taken from the MDS-UPDRS. For this study, the author was the examiner.

Both of the subject's arms were tested, one after the other. Each subject also repeated each symptom assessment for a non-mimicked and mimicked test.

Subjects were shown by the author how best to mimic the symptoms. The author has attended Parkinson's disease clinics at Charing Cross Hospital, London.

Rigidity Assessment: Rigidity is only judged through slow passive motion by the examiner on the limb of the subject. Only the arms were examined during this study, specifically rigidity about the elbow. The subject started with their arm straight and relaxed, the examiner then moved the forearm into flexion and extension using the force sensor handle. The force sensor recorded any resistive forces to this motion. The IMUs were required to record both the angular velocity and displacement between the forearm and upper arm during the assessment. The force, angular velocity and angular displacement were used to model the amount of rigidity. This motion was repeated five times. This set of repetitions was then repeated a further two times with a 5 s break in-between each set.

Bradykinesia Assessment: Once the rigidity assessment was completed, the force sensor and handle were removed from the subject's arm leaving only the pair of IMUs. People with Parkinson's disease have much more difficulty and take a prolonged amount of time to pronate and supinate their wrists, an observation of bradykinesia. After a demonstration, the subject was asked to pronate and supinate their wrist for five repetitions. A 5 s break was taken before repeating the set of repetitions a further two times. The IMUs recorded the angular velocity during the assessment which was used to model the amount of bradykinesia.

Tremor Assessment: Three separate sub-assessments were conducted to quantify the three different types of tremor; postural, kinetic and rest tremor.

Postural tremor can occur when a subject is asked to hold a certain posture. Subjects were asked to hold out their arm for five seconds during the postural tremor assessment. The subject's arm had to be oriented such that their palms were facing downwards, wrists were straight and fingers were comfortably spread. Kinetic tremor can occur when a subject is asked to concentrate on moving a limb to a target location. Kinetic tremor assessment began by asking the subject to stretch out their arm to touch the examiner's finger with their index finger. The examiner then instructed the subject to move their finger to their own nose and back to the examiner's finger. The tremor in PD patients can be present throughout the motion or as the tremor reaches the intended target (examiner's finger or their own nose). The task was performed slowly to ensure no tremor was masked. Tremors can also being observed during a resting state, i.e. resting tremor. The subject was asked to sit comfortably in the chair, with their arms on the armrest and their fit supported by the floor. A break of 5 s was then given before repeating each set of repetitions a further two times. The IMUs were able to record accelerations to model the amount of tremor.

2.4 Analysed Parameters

To model and quantify rigidity, the torque and elbow angle data can be found with these sensor measurements to allow us to find impedance and VEPs of the arm. Angles between the forearm and upper arm were calculated by finding the difference in orientation of the two IMUs. The angular velocity was given from the gyroscopic readings.

Using the force from produced from the force transducer, a torque could be calculated from the product of the force and the moment arm (distance from the elbow pivot to force sensor placement). A torque model was presumed to have both elastic and viscous components and any components concerning acceleration were ignored due to the low frequency nature of the tests [1–3]. Multiple linear regression was then performed with the torque (T), angular displacement (θ) and velocity ($\dot{\theta}$) values to extract elastic stiffness (K), viscous stiffness (B) and constant (e) values as shown in (1) below:

$$T = K|\theta| + B|\dot{\theta}| + e \tag{1}$$

VEPs were defined as the elastic stiffness and the viscous stiffness. Impedance (Z) was then calculated as the vectorial sum of the elastic and viscous stiffness [1–3] using (2):

$$Z = K + B\omega \tag{2}$$

where ω is the peak-to-peak frequency of the limb during an assessment. The average frequency for each assessment was used as the peak-to-peak frequency to calculate the impedance.

The RMS angular velocity from the gyroscopic data of the IMUs was utilised to quantify and model bradykinesia and the accelerometer data of the IMUs was used to identify and model tremor. Fast Fourier Transform (FFT) and peak power analysis were utilised to find instances of postural, kinetic and rest tremor.

2.5 Statistical Analysis

To evaluate if the sensor suite could identify a significant difference between the non-mimicked and mimicked data using the analysed parameters, an independent t-test was used. If $p \leq 0.15$, this was interpreted as a significant difference between the non-mimicked and mimicked data. All statistical analysis was undertaken in Matlab.

3 Results

3.1 Rigidity

Both impedance and VEPs were parameters used in this study to quantify rigidity. Force data were filtered using a fifth-order, low pass Butterworth filter with cut-off frequency at 20 Hz to remove any high frequency noise in the signal and to avoid aliasing when resampling. Force and IMU data were re-sampled to 125 Hz.

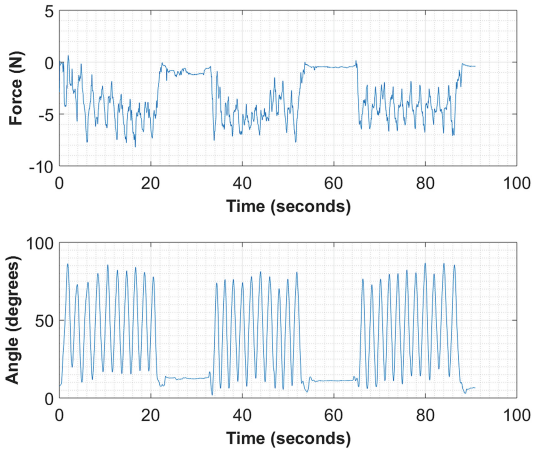

Fig. 2. Force and angle displacement for a non-mimicked test

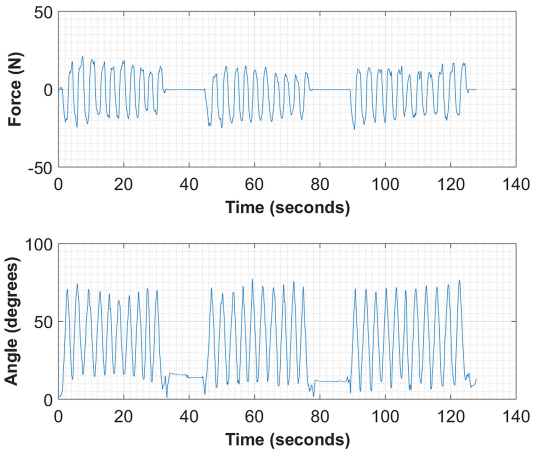

Fig. 3. Force and angle displacement for a mimicked test

Figure 2 shows the raw data for a test without any mimicked symptoms and Fig. 3 shows the raw data for a test with mimicked symptoms. The distinct differences in force magnitudes visually portrays the usefulness of the sensors in distinguishing between a non-mimicked, baseline reading (MDS-UPDRS = 0) and a mimicked reading (MDS-UPDRS $\neq$ 0). The impedance and VEPs were then calculated from the raw data to observe the presence of rigidity.

An independent t-test with unequal variances was conducted to assess the effectiveness of impedance and VEPs in detecting rigidity. The impedance and VEPs were the dependent variables for the test whilst the test type was the independent variable. The null hypothesis, H_0, is defined as both the non-mimicked

and mimicked data having equal means, i.e. the sensor suite was unable to recognise any differences. The viscosity parameter produced a p-value of 0.0131 and the impedance parameter produced a p-value of 0.0092 averaged across all subjects. The elasticity parameter had a very high p-value of 0.8105 averaged across all subjects. H_0 was therefore rejected for the viscosity and impedance parameters as $p \leq 0.15$, meaning that both parameters successfully differentiated between the two tests. Elasticity was not a good parameter in distinguishing between the two tests.

3.2 Bradykinesia

The gyroscopic data for one subject is shown below in Figs. 4 and 5. Visually, a difference was observed for the two tests during the bradykinesia assessment. Before any analysis, the recorded gyroscope data was filtered using a fifth-order, low pass Butterworth filter with a cut-off frequency of 5 Hz. This was needed to remove any high frequency noise and to discard any movements related to tremor. Rotational velocities of up to 400°/s and an average velocity of 79°/s were recorded for non-mimicked tests. Rotational velocities of up to 50°/s and an average of 30°/s were recorded for mimicked tests.

An independent t-test with unequal variances was conducted to quantify any significant differences between the non-mimicked and mimicked bradykinesia

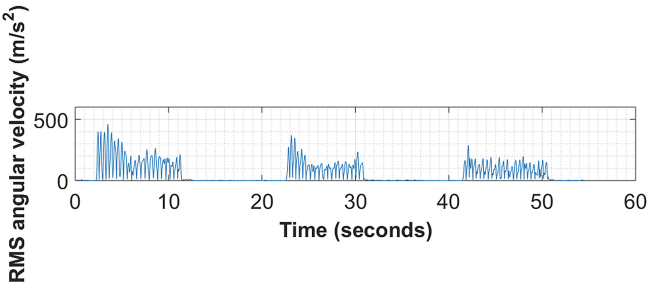

Fig. 4. RMS angular velocity of the wrist for a non-mimicked test

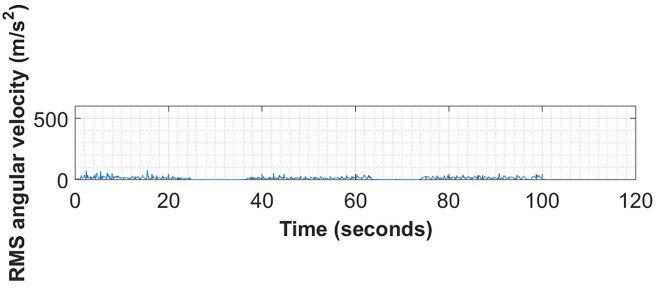

Fig. 5. RMS angular velocity of the wrist for a mimicked test

data. The average RMS angular velocity was used as the dependent variable and the test type was used as the independent variable. The null hypothesis, H_0, was defined as both types of test having equal means. Using the average RMS angular velocity parameter, a p-value of 0.0938 was produced. H_0 was hence rejected as $p \leq 0.15$. This verified that significant differences were observed between the non-mimicked and mimicked data.

3.3 Tremor

A fifth-order, band pass Butterworth filter with cut-off frequencies of 3–12 Hz was used because it has been recognised that Parkinsonian tremor occurs at this defined frequency band [9,10]. Tremor data were then Hamming windowed and zero-padded to isolate the relevant frequencies. Data from each tremor sub-assessment was analysed in an identical fashion.

The FFT of an accelerometer signal from the postural tremor assessment for one subject is shown below in Figs. 6 and 7. FFTs from all sub-assessments of tremor portrayed similar results. Significant tremors were produced during the mimicked tests and these were observed to be several magnitudes larger than their non-mimicked counterparts. This suggested that the peak magnitudes in the defined frequency band were an excellent indicator to detect the presence of tremor.

An independent t-test was conducted to statistically assess whether the peak magnitudes from FFTs of the accelerometer signal were able to distinguish differences between the non-mimicked and mimicked data. The peak magnitude for the FFT of the acceleration signal was used as the dependent variable and the test type was the independent variable. The dependent variable was restricted to the aforementioned tremor frequency band of 3–12 Hz. The null hypothesis, H_0, was defined as both test types having equal means. The postural tremor

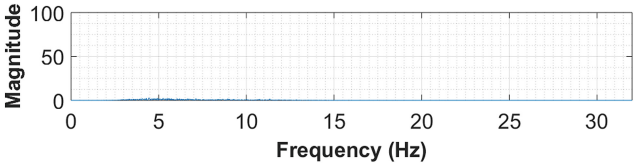

Fig. 6. FFT for a non-mimicked postural tremor test

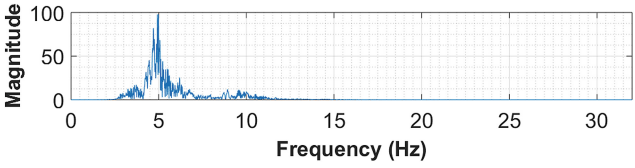

Fig. 7. FFT for a mimicked postural tremor test

t-test had a p-value of 0.0294, the kinetic tremor t-test had a p-value of 0.0028 and the rest tremor t-test had a p-value of 0.1045. All tremor sub-assessment t-tests had a p-value ≤ 0.15 which allowed the rejection of the null hypothesis.

4 Discussion

There were two reasons this study was conducted. Firstly, to record baseline results to compare with future tests on Parkinson's disease subjects. Baseline results are results from healthy control subjects during the non-mimicked tests essentially with a MDS-UPDRS score of zero. Secondly, the device needed validation by assessing working models to identify symptoms of Parkinson's disease. The results have shown that the device is capable in distinguishing between non-mimicked and mimicked results for all primary Parkinsonian symptoms. Following the outcome of this study, trials on PD subjects will next be conducted using the sensor suite.

4.1 Rigidity

Subjects were asked to stiffen their arm during the mimicked test. Out of the three primary symptoms, it is the most difficult to identify because of the external assistance needed. To assess whether rigidity is present in each subject, impedance and VEPs were analysed.

Mechanical impedance was calculated using (2). It has been highlighted that measures derived from torque, such as mechanical impedance, should depend significantly on the movement velocity and hence cannot properly represent the features of Parkinsonian rigidity [4]. However, throughout the rigidity assessment, constant velocity movements were used. Mechanical impedance was hence found to be an excellent differentiator between non-mimicked and mimicked tests with a p-value of 0.0092. Impedance had a smaller p-value than viscosity for the independent t-test. Further trials with a larger cohort of subjects are required to fully understand why this occurred. One potential reason could be the magnifying factor of the peak-to-peak frequency. Since the impedance was more influenced by the product of the viscosity and the peak-to-peak frequency, rather than elasticity, the impedance could equate to larger differences because of this magnifying factor.

The viscosity parameter was found to be slightly worse at differentiating between the two tests with a p-value of 0.0131. Elasticity did not reject the null hypothesis and had equal means for both the non-mimicked and mimicked tests. Impedance is defined as the vectorial sum of both viscosity and elasticity and yet it managed to distinguish between non-mimicked and mimicked tests. Elasticity therefore had little influence on impedance and this suggests that the magnitudes of elastic stiffness were much smaller compared to viscosity and impedance.

It has been suggested that viscosity was a better identifier of rigidity compared to mechanical impedance because it does not rely on movement velocity [4,11]. However, this study has shown that there is negligible difference between

the viscosity and impedance when identifying rigidity between non-mimicked and mimicked tests. In addition, because of the torque model used to extract viscosity and elasticity values, viscosity actually relies on the movement velocity used in their studies. Larger cohort trials on PD subjects are required to distinguish the better performance index with this device.

The rigidity assessment in this study does have limitations. The device currently only identifies rigidity at the elbow. Rigidity can be found at other joints such as the wrist, knee and ankle joints. Future iterations of the device will incorporate functionality to be used on other joints. Moreover, further tests are required to detect rigidity at the higher resolution scale of the MDS-UPDRS. Higher resolution quantification can allow for more accurate and efficient treatments to symptoms.

4.2 Bradykinesia

Bradykinesia is another cardinal symptom of Parkinson's disease. One of the assessments for bradykinesia in the MDS-UPDRS protocol observes the speed at which the patient can pronate and supinate their wrist. In clinic, the patient is asked to do this as quickly as possible. As aforementioned, the first test was the non-mimicked test, whilst the second test was a symptom-mimicked test. In this bradykinesia assessment, subjects were asked to pronate and supinate their wrists slower in the mimicked test and IMUs were used to record the angular velocity of the wrists. RMS angular velocity has been shown to be a good performance index for bradykinesia in PD patients [5,6].

An independent t-test with unequal variances was conducted to test whether the sensor suite's algorithm can determine if there was a distinct difference between the non-mimicked and mimicked test. The p-value for the t-test was 0.0938 which indicates that the null hypothesis can be rejected, and that there was a significant enough difference between the RMS angular velocities of the two tests. Other assessments such as finger tapping would be considered for these trials [12]. If lower limb bradykinesia were to be explored, toe-tapping tests would also have to be considered [13,14]. Other parameters, such as peak power analysis and angular displacement will be contemplated for future tests on PD patients as an attempt to improve bradykinesia detection.

4.3 Tremor

Tremor in Parkinson's disease can be sub-categorised into postural, kinetic and rest tremor. As such, all three of these subcategories were tested in this study using the PDD. Postural tremor occurs when the patient is subject to any effects of gravity, i.e. holding their hand in the air, kinetic tremor occurs when the subject is asked to move their limb towards a target and rest tremor is observed when a patient is not doing anything.

Tremor has been detected in PD patients using accelerometers [7,8,10]. It has been suggested that peak power of accelerations was the best indicator of a

tremor state [7,10]. Peak power analysis of the accelerations from the IMUs was used to identify tremor in this study.

The analysis for each type of tremor was identical. It was promising to observe that the peak power for every mimicked test occurred between the recommended 3–12 Hz range as suggested by the literature. This shows that healthy subjects were able to mimic tremor symptoms of PD patients very well in all tremor sub-assessments.

The FFT for non-mimicked and mimicked tests suggest that peak power analysis is an excellent detector for all types of tremor. The mimicked peak power magnitudes are at least a factor of 10 larger than their non-mimicked counterparts. Each of the subcategories of tremor have significantly different magnitudes between the non-mimicked and mimicked tests with p-values below 0.15. The sensor suite was able to distinguish successfully between mimicked and non-mimicked tests.

5 Conclusion

It was concluded that the system presented could distinguish between non-mimicked and mimicked tests for all symptom assessments, with very convincing differences. The sensor suite presented has become a platform to truly begin assessing all primary symptoms of Parkinson's disease in one session, rather than one at a time. Moreover, this study is a mandatory step towards closing the loop for DBS therapy using external sensors and improving rehabilitation with current rehabilitation robots with the potential to provide live feedback to the user. Future studies on PD subjects will include more detailed symptom detection algorithms. This is necessary because of the higher resolution scale of the MDS-UPDRS.

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