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Automated assessment of symptom severity changes during Deep Brain Stimulation (DBS) therapy for Parkinson's disease

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Abstract— **Deep brain stimulation (DBS) is currently being used as a treatment for symptoms of Parkinson's disease (PD). Tracking symptom severity progression and deciding the optimal stimulation parameters for people with PD is extremely difficult.**

This study presents a sensor system that can quantify the three cardinal motor symptoms of PD - rigidity, bradykinesia and tremor. The first phase of this study assesses whether data recorded from the system during physical examinations can be used to correlate to clinician's severity score using supervised machine learning (ML) models. The second phase concludes whether the sensor system can distinguish differences before and after DBS optimisation by a clinician when Unified Parkinson's Disease Rating Scale (UPDRS) scores did not change. An average accuracy of 90.9 % was achieved by the best ML models in the first phase, when correlating sensor data to clinician's scores. Adding on to this, in the second phase of the study, the sensor system was able to pick up discernible differences before and after DBS optimisation sessions in instances where UPDRS scores did not change.

I. Introduction

Parkinson's disease is a degenerative, neurological condition impacting millions of patients worldwide. The main motor symptoms include tremor, bradykinesia, rigidity, as well as issues such as speech impairment and bladder control. There is no cure for PD, however treatments are available depending on the symptom severity.

Tremor is the involuntary shaking of a limb, such as the arm or leg. The clinician assesses this particular symptom visually. More severe tremors are seen to have a much larger range of periodic motion, i.e. large peak-to-peak amplitudes. Tremors in this study were split into three subcategories - kinetic tremor, postural tremor and rest tremor. Kinetic tremor occurs during an action by the patient, postural tremor happens when the patient is holding a posture and rest tremor occurs when the patient is in a resting position.

Bradykinesia is defined as slow movement. It restricts the speed of intended movement of the limbs. When this symptom affects the arm, it can be assessed in the clinic by observing the pronation and supination of the wrist or the speed and frequency of tapping their finger and thumb together. Slow speeds and small ranges of motion during this assessment indicate severe bradykinesia.

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Rigidity translates to stiffness in the joints; commonly the elbow, wrist, knee or ankle. It occurs because of an unwanted increase in muscle tone. The severity of this symptom is judged by an external, passive movement of the affected limb.

In the early stages of PD, oral medication is typically prescribed, whilst in the more advanced stages, a combination of oral medication and DBS is used. DBS involves the surgical placement of electrical stimulators in the deep brain regions, typically the globus pallidus pars interna (GPi) or subthalamic nucleus (STN), to restore function.

Whilst DBS is a firmly established treatment for PD, selection of optimal stimulation parameters (amplitude, pulse width, waveform, frequency and contact) is complex and clinically demanding. Understanding and quantifying how DBS correlates with both symptom severity and improvements, cannot be done empirically. Neurologists are forced to assess the look and feel of symptoms and must manually adjust stimulation parameters based on intuitive judgement via a scoring scale called the UPDRS. The lack of real quantifiable and detailed feedback on patient response to DBS parameter adjustment means clinicians are unable to keep track whether a particular DBS setting was an improvement, and, if so, by how much in comparison to the last DBS setting [1]. These issues will likely compound as surgical practice moves to electrodes with ever greater contact numbers and ageing patient populations increase [2].

A. Current state of the art for symptom measurement

Metrics such as viscoelastic properties (VEPs) and impedance of limbs have been derived from sensor data to quantify rigidity on the elbow and wrist, and to find correlations to the UPDRS scores [3]–[6]. Electromyography (EMG) measurements have shown promise at quantifying rigidity in Parkinson's disease as well [7].

There have been studies using features from motion sensors such as accelerometers and gyroscopes to quantify bradykinesia [8]–[10]. RMS angular velocity was a popular feature used to correlate to the clinician's severity score delivering promising results.

Accelerometers have been the most frequently utilised sensor to measure tremor [11]–[14]. This is because accelerometers encapsulate all the characteristics of tremor to measure how severe it is, such as the amplitude and frequency.

Previous studies have suggested the use of an all-in-one sensor system - a system that measures all three of the

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cardinal motor symptoms [15], [16]. However, these systems have yet to be tested on subjects with Parkinson's disease.

The aforementioned studies highlighted the method of creating specific and tailored models for each symptom using sensor data, however some groups have used ML to model symptom severity. ML algorithms have specifically been used to measure non-motor symptoms such as rapid eye movements [17] and motor symptoms, such as bradykinesia [18], [19] from sensor data.

In this investigation, we report the development and initial testing of a sensor system to offer specific information on symptomatic response of PD symptoms to DBS parameter adjustment during therapy sessions. The system focuses on the quantification of tremor, rigidity and bradykinesia using supervised ML models.

B. Contributions of Investigation

The contributions from this paper are two-fold. Firstly, a sensor system, including original bespoke hardware components, has been developed to record kinetic data from the arm during physical assessments of Parkinson's disease. Specifically, the acceleration, gyroscope, muscle activity and resistive force data have been recorded during this study. ML classification models were developed and implemented to assess whether the data recorded from the sensor system was able to correlate to the correct severity scores of the three cardinal symptoms of PD as given by the clinician after each assessment. Secondly, the system was assessed to find whether it can pick up differences due to a change in DBS parameters, even if the severity score of the subject given by the clinician had not changed.

We believe these results demonstrate the feasibility of developing a sensor system that can be used to track symptom variations in PD more frequently in clinic or at home, and lay a foundation for a home-based system where DBS parameters could be adjusted out-of-clinic.

II. Methodology

A. Sensor system

The sensor system designed for this investigation, extending pilot experiments of our past work [16], [20]–[22], consisted of three sensing modalities; inertial motion, muscle activity, and force. The system, depicted in Fig. 1 consists of three 9 degree of freedom inertial measurement units (IMUs), 4 mechanomyographic (MMG) sensors and a force sensor.

The IMUs contain a tri-axial accelerometer, a tri-axial gyroscope and a tri-axial magnetometer. All IMUs were designed and fabricated by our team in the Biomechatronics Lab at Imperial College London. A bespoke IMU was necessary to incorporate MMG sensor inputs into the system in real-time. The first IMU was placed on the upper arm, the second IMU on the forearm and the third IMU on the hand. This was necessary to fully track the movement of the arm in 3D space. IMUs were sampled at a rate of 100 Hz.

Symptomatic assessment of rigidity, bradykinesia and tremor demanded a steady trace of muscle activity during physical assessment. We chose MMG, a measure of the acoustic or vibrational artefact of muscle movement, as a means of recording this information. MMG was chosen over EMG for ease of use in application for therapy sessions and for future home use. The system used 4 MMG sensors; 2 on the upper arm and 2 on the forearm. The MMG sensors on the upper arm were placed on both the biceps brachii and the triceps brachii. On the forearm, an MMG sensor was placed on the flexor digitorum superficialis and another on the flexor carpi radialis. All MMG sensors were sampled at 1000 Hz.

A force sensor (OMD-20-FE-200N, OptoForce) was used to track the resistive force during the rigidity assessments. The force sensor was sampled at a rate of 100 Hz.

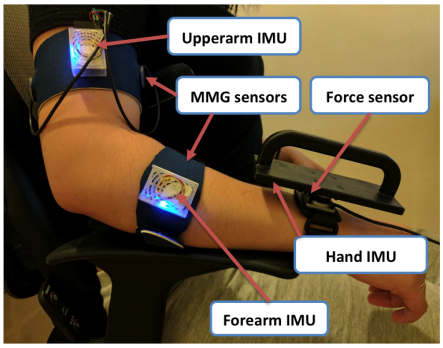


Fig. 1: The full sensor system set up on a subject's arm. In total, 3 IMUs, 4 MMGs and a force sensor were used for this study.

B. Subjects

Subjects with PD who are receiving DBS treatment will be recruited for this study. Subjects with rigidity, tremor, bradykinesia or some combination of the rigidity, tremor and bradykinesia were specifically asked to participate in this study. Participants followed their regular medication routine as taking them off their routine may have lead to injuries and unwarranted difficulties. Seven PD subjects participated for this particular part of the study and their corresponding symptom details for the whole study, including the subtypes of each symptom (i.e. kinetic, postural and rest tremor), are shown in Table I. In total, 234 data sets (13 separate trials x 6 symptoms x 3 repetitions) were captured. All subjects consented to participating in the study and ethical approval was received from the HRA to conduct the study.

C. Experimental protocol

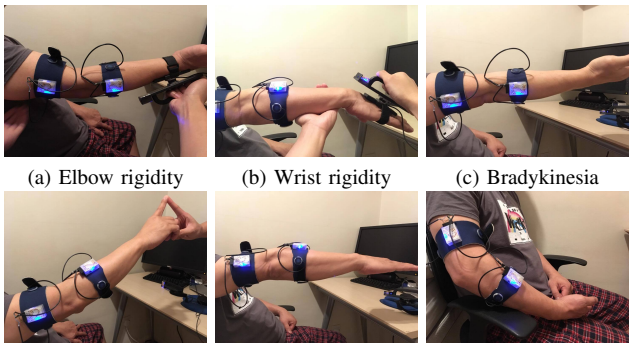
The subject was seated with the sensors attached to the most severely affected arm. The procedure followed assessments extracted from Part III of the UPDRS protocol that measures each of the primary motor symptoms. Each assessment during this trial was repeated 3 times. A clinician then rated the UPDRS score for each symptom. When the clinician believed that an improvement on symptoms was available, the clinician then attempted to optimise the DBS settings of certain subjects after which, the whole procedure of assessments was repeated again. The following

TABLE I: A list of subjects with their associated UPDRS scores for the whole study given by the clinician.

Patient ID	UPDRS			No. of completed trials
	Rigidity	Bradykinesia	Tremor	
001	0-2	1-3	0-3	2
002	0-1	1-2	0-1	3
003	0	0	0	1
004	0	1	0-1	1
005	2-3	2	0	2
006	2-3	2	0-3	1
007	0-2	0-1	0-1	3
Total no. of completed trials				**13**

assessments (demonstrated in Fig. 2) were included in this study whilst the subject was sitting:

1) Elbow rigidity - Rigidity is observed from passive motion, which in this case was provided by a clinician. The subject initially had the arm being tested fully extended and relaxed. The clinician then proceeded to move the subject's forearm into the fully flexed position and back again to the fully extended position using the force sensor handle. This flexion and extension of the arm was repeated five times per set and each set was completed three times.
2) Wrist rigidity - The same process was followed from the elbow rigidity assessment except that the force sensor was attached around the palm of the hand. The wrist, instead of the forearm, was flexed and extended during this assessment.
3) Bradykinesia - The force sensor and handle were then removed for the bradykinesia and tremor assessments. People who suffer from bradykinesia have difficulty with the pronation and supination of their wrists at a normal speed and to a full range of motion. One pronation and supination movement was repeated five times per set and each set was completed three times.
4) Kinetic (intentional) tremor - The subject was asked to place their index finger, from the arm being assessed, on their nose. The subject was then asked to move their finger to the clinician's finger, which was at a distance of approximately 50-60 cm away from the subject's nose, and back again to their nose. This action was repeated five times per set and each set was repeated three times. Kinetic tremor can be activated when a patient intentionally moves their hand towards a distant but reachable target.
5) Postural tremor - The subject was then asked to hold their arm out directly in front of them for one set which lasted ten seconds. This posture set was repeated three times overall with a break in-between each set. This type of tremor is activated when a posture is being held.
6) Rest tremor - The subject was asked to rest their arms and hands on their laps with their palms facing towards the ceiling for ten seconds. This was repeated a further two times.



(a) Elbow rigidity (b) Wrist rigidity (c) Bradykinesia

(d) Kinetic tremor (e) Postural tremor (f) Rest tremor

Fig. 2: A demonstration of the physical examinations used for each symptom with the sensor system attached to the subject's arm.

D. Preprocessing of data

Before any feature extraction began, relevant signals were filtered. It has been understood that the dominant frequencies of tremor occur from 3-11 Hz [23]. A band pass 5th order Butterworth filter from 2-15 Hz was therefore used to encapsulate all the essential tremor data. In addition to this, a band pass 5th order Butterworth filter from 20-30 Hz was used on all data recorded from MMG sensors. The dominant frequencies of MMG data has been described to be in the region of 22 to 28 Hz [24].

E. Feature extraction and selection for ML models

Individual features were extracted from each of the individual sensor components of the system. The sampling rate for all sensors were kept constant for each trial but the sample size for each trial of rigidity, bradykinesia and kinetic tremor varied due to differing assessment completion times for each subject. The mean of each feature (MF) and standard deviation of each feature (SDF) from the data recorded from the sensors were calculated using:

$$MF = \frac{1}{N}\sum_{i=1}^{N} a_i \tag{1}$$

$$SDF = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N} |a_i - MF|^2} \tag{2}$$

where a_i is the feature vector and this is either the acceleration, angular velocity or the orientation of the IMU, the force data or the MMG sensor data. All in all, a total of 92 features were extracted for each assessment.

Though all of these features were calculated, using all 92 features to train a model would lead to unnecessary over fitting and hence reduced accuracy. Instead, features were selected based on what was viewed as useful for both the symptom being assessed, and the method of assessment. Table II shows a summary of all features used for each symptom examination.

TABLE II: A list of all the symptoms examined with the corresponding features selected for the ML models.

Symptom	Features selected
Elbow rigidity	- Mean upper arm MMG - Standard deviation upper arm MMG - Mean force - Mean forearm angular velocity - Standard deviation forearm angular velocity
Wrist rigidity	- Mean forearm MMG - Standard deviation forearm MMG - Mean force - Mean hand angular velocity - Standard deviation hand angular velocity
Bradykinesia	- Mean forearm angular velocity - Standard deviation forearm angular velocity - Mean forearm MMG - Mean upper arm angular velocity - Standard deviation upper arm angular velocity - Mean upper arm MMG
Kinetic, Postural and Rest Tremor	- Mean forearm acceleration - Standard deviation forearm acceleration - Mean forearm MMG - Mean upper arm acceleration - Standard deviation upper arm acceleration - Mean upper arm MMG

F. Phase I - Classification

For this study, the patient data that was collected by the sensor system needed to be categorised accordingly into different severity scores as given by the clinician. The severity scores given by the clinician were based from the UPDRS; a tried, tested and validated scale used universally to assess Parkinson's disease symptoms. Severity scores for motor symptoms such as tremor, bradykinesia and rigidity are given a score from 0, increasing by 1, all the way up to 4. 0 indicates that the symptom severity is nil and 4 indicates extremely severe. There are drawbacks with the UPDRS, such as subjectivity from clinicians and the low resolution of the scale (only 5 stages).

Three supervised machine learning models were used to compare and assess which technique performed best with the sensor data collected. All classification models were built in Matlab using the Classification Learner Application. A 5-fold cross-validation was used when training and testing the model. An accuracy percentage is then given based on how well the model can predict outcomes from the testing dataset.

The three classification methods used in this study were: 1) Simple decision trees, 2) Multi-class support vector machines (SVMs) and 3) K-nearest neighbours (kNN):

1) Simple decision trees: Simple decision trees are a subtype of decision trees. Simple trees make very coarse and broad decisions between classes allowing a maximum number of splits of 4 between nodes. Fig. 3 highlights a model specific to categorising scores for bradykinesia using only three features.

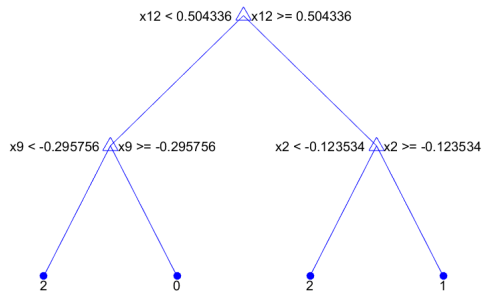


Fig. 3: A sample simple decision tree model for classifying bradykinesia into categories of UPDRS scores using the mean forearm angular velocity, the mean upper arm angular velocity and the standard deviation of quaternions recorded from the forearm.

2) Multiclass SVMs: Multi-class SVMs with a linear kernel were utilised for this study to categorise sensor data. The optimal separation, and hence optimal model, between the two groups is achieved by maximising the distance between the hyperplane and the nearest data point from each group. A hyperplane is defined as:

$$g(x) = \overrightarrow{w}.\overrightarrow{x} + b \tag{3}$$

where $\overrightarrow{w}$ are the weights, $\overrightarrow{x}$ are the sensor data and b is the bias. For binary classification, that is separating data into only two classes, one class is defined such that $g(x) \geq 1$ and the other class so that $g(x) \leq -1$. The distance, z, between the nearest data points of two groups is defined as:

$$z = \frac{2}{||\overrightarrow{w}||} \tag{4}$$

and hence to maximize the distance between the two groups of data, $\overrightarrow{w}$ should be as small as possible. Since the data needed to be categorised into more than two classes (up to five classes with the UPDRS), a one-vs-one multi-class method was used.

3) K-nearest neighbours: The kNN algorithm was also implemented for this study to categorise the patient data. For this study, k = 1, so the patient data were classified based on the single nearest data point, i.e. if the nearest data point had a UPDRS score of 1, the data point under question would then be classified as UPDRS = 1 as well. Essentially, data points can be categorised depending on which region it landed in. A region can be defined as the space occupied by each individual training data point. A region, R_i, is defined as:

$$R_i = [x : d(x, x_i) < d(x, x_j), i \neq j] \tag{5}$$

where x is the data point to be classified, x_i is the nearest neighbour and x_j is the second nearest neighbour. If the distance from x to x_i is smaller than the distance of x to

x_j, then the data point x falls into the region of x_i and is categorised into the same class as x_i.

G. Phase II - Identifying subtle improvements

The second phase of this study ventured into assessing subtle changes during DBS alterations. During the study, there were three instances where the clinician changed the stimulation parameters to improve one particular symptom, but the severity score had remained the same. Details of these instances are given in Table III.

TABLE III: Instances where UPDRS scores did not change after DBS optimisation.

Instance	Symptom	Feature used	UPDRS score before and after
1	Elbow rigidity	Mean normal force	3
2	Wrist rigidity	Mean normal force	2
3	Bradykinesia	Mean roll angular velocity	2

To distinguish whether there was an improvement in symptom severity which was not portrayed from the UPDRS score, a paired t-test with a significance value of 0.1 was conducted to assess differences in means of features before and after DBS changes. The mean of the normal force to track both elbow and wrist rigidity and the mean of the angular velocity in the roll axis to track bradykinesia were the features selected for this phase of the study. These were the most dominant features that represented each relative symptom. A relatively large significance level was used to highlight any potential differences picked up by the sensor system.

III. Results

A. Phase I

Of the seven subjects, a variety of severity scores were given for each symptom ranging from 0 to 3. Table IV formalises all the results from the first phase of the study for all symptoms. The best ML models are highlighted in bold and the average accuracy performance from these best models for all symptoms was 90.9 %. Considering that this is the first sensor system that attempts to quantify the three cardinal motor symptoms of Parkinson's disease, as well as the first all-in-one system to be tested on subjects with PD, the results are promising.

The fine kNN performed best out of the three ML models achieving the highest accuracy for 5 out of the 6 symptoms. The accuracies for the tremor ML models are consistently below 90 % regardless of the model selected, so there are still potential improvements that can be made here.

B. Phase II

Results from phase II of the study are presented in Table V. For each of these symptom assessments, the clinician scored the severity of the symptom similarly before and after the DBS adjustments. The sensor system was able to distinguish differences from before and after DBS parameter changes for the first two instances.

TABLE IV: Average accuracies of the supervised machine learning models for each symptom.

Symptom	Simple Tree (%)	Linear SVM (%)	Fine kNN (%)
Elbow rigidity	66.7	79.5	**100**
Wrist rigidity	77.5	77.5	**95.0**
Brady-kinesia	70.0	77.5	**92.5**
Kinetic tremor	84.6	82.1	**87.3**
Postural tremor	73.2	**82.9**	78.0
Rest tremor	78.0	82.9	**87.8**

TABLE V: P-values from paired t-test for identifying changes after DBS optimisation.

Instance	Symptom	p-value
1	Elbow rigidity	0.079
2	Elbow rigidity	0.039
3	Wrist rigidity	0.435

IV. Discussion

Phase I of the study showed that the sensor system was able to classify symptom severity according to the UPDRS score given by the clinician. The sensor system was able to predict UPDRS scores with an average accuracy of 90.9 % for all symptoms across seven subjects. Categorisation performance of the rigidity and bradykinesia symptoms was much higher than their tremor counterparts averaging 95.8 % compared to 86.0 %.

There are a number of contributing factors as to why this may have occurred. Firstly, the features that were selected, the mean and standard deviations of accelerations and MMGs on the arm, may not have been the best suited to classify the tremor accordingly. A more rigorous approach to selecting features for tremor will have to be employed and failing any improvement from this, new features and potentially additional sensors will then be considered. New features such as the skewness of acceleration, jerk (derivative of acceleration) and a combined metric of acceleration and MMG will be contemplated in future analysis. Secondly, a future study using different ML algorithms using the same feature set will be considered to see if any improvements can be found. Finally, a more sophisticated preprocessing filter will be investigated in future studies to clean the data better before being used for the ML models.

Despite this, an average accuracy of 90.9 % is still an achievement. This type of classification, to the author's knowledge, with an all-in-one sensor system, has not been tested on subjects with PD before [15], [16].

The second phase of the study shows that there are potential difficulties of rating symptom severity using the UPDRS, more specifically with rigidity symptoms. This raises an issue with the current standard UPDRS being too low resolution. The clinician concluded that there was an improvement in the symptom severity and the sensor system also found differences, more so for instances 1 and 2 from Table V with p-values < 0.1, after the DBS settings optimisation. These improvements however could not be reflected using the current standard UPDRS. A larger sample size will be required to further assess this potential issue.

The UPDRS has five stages of severity only. Treatments, and treatment dosages in the case of oral medication, are solely based on how severe the clinician rates each symptom. By having a more sensitive method of quantifying symptom severity, such as the proposed sensor system, small improvements can be measured and recorded better and as a result, people with PD will have access to a better quality of life.

The study has validated the use of the sensor system to be used as a feedback system to help clinician's have a detailed review of a patient's symptoms.

V. Conclusion

The purpose of this research was two-fold, to firstly identify whether the sensor system could categorise data based on a clinician's score and secondly, to assess any differences based on sensor readings, from before and after DBS reprogramming sessions, even if the clinician's score has not changed. The results from both of these phases of the study are very positive and warrant further investigation.

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