Objective Evaluation of Bradykinesia in Parkinson's Disease using Evolutionary Algorithms

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Abstract: Bradykinesia, a slowing of movement, is the fundamental motor feature of Parkinson's disease (PD) and the only physical sign that is obligatory for diagnosis. The complex nature of Bradykinesia makes it difficult to reliably identify, particularly as the early stages of the disease. This paper presents an extension of previous studies, applying evolutionary algorithms to movement data obtained from the standard clinical finger tapping (FT) test to characterise Bradykinesia. In this study, hand pronation-supination (PS) and hand opening-closing (HO) tasks are also considered. Cartesian Genetic Programming (CGP), is the evolutionary algorithm used to train and validate classifiers using features extracted from movement recordings of 20 controls and 22 PD patients. Features were selected based on the current clinical definition of Bradykinesia. The results show the potential of HO and PS to be used as effective classifiers with an accuracy of 84%. Discriminative features were also investigated with the possibility of informing clinical assessment.

1 INTRODUCTION

Bradykinesia, meaning slowness of movement, is the only clinical sign that is mandatory for the diagnosis of Parkinson's Disease (PD) (Heldman et al. 2011). The terms akinesia (absence of movement), bradykinesia (slowness of movement), and hypokinesia (decreased amplitude), are all used interchangeably to describe the most prominent phenomena of Parkinsonism. The conditions they describe are usually referred to collectively as **bradykinesia** (Figure 1). This symptom might have the highest potential as a motor progression marker of Parkinson's disease (Maetzler et al. 2009). The complex nature of Bradykinesia itself is one of the reasons that makes it difficult for clinicians and neurologists to be certain of its existence in the early stages of Parkinson's disease. Clinicians look for signs of bradykinesia by observing a patient's ability to perform rapid, repetitive, alternating movements of the hand using tasks such as finger taps, toe taps, hand grips and hand pronation–supination (Jankovic 2008). The gold standard for clinical evaluation is the Unified Parkinson's Disease Rating Scale, UPDRS, and its modified version, MDS-UPDRS (Goetz et al. 2008). It remains unclear how slowed movements due to physiological ageing are different from the bradykinesia seen in parkinsonian conditions. A better understanding of characteristics of bradykinesia and how it differs between these groups can be used to inform clinical assessments towards conforming early diagnosis.

Finger tapping (FT) is a popular task that has been used many times in studies to evaluate Bradykinesia in PD. Several methods have been used to optimise FT data recorded by movement sensors in studies that use statistical tests to compare movement features of PD patients against healthy controls (Dunnewold et al. 1997) (Jobbágy et al. 2005) (Yokoe et al. 2009) (Espay et al. 2011) or with other movement disorders (Ling et al. 2012). Alternatively, popular statistical machine learning methods such as support vector machine (SVM) is claimed to achieve better classification on FT movement data. (Martinez Manzanera et al. 2015) (Patel et al. 2009).

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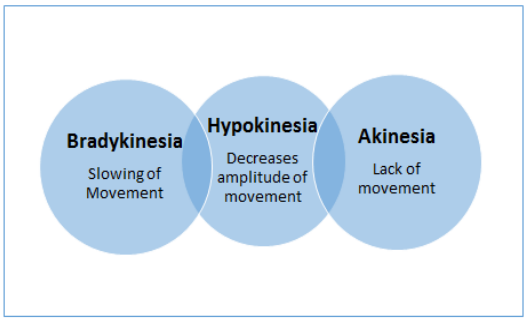

Figure 1: Descriptions of Bradykinesia. (Fernandez et al. 2014).

Our group have successfully used Evolutionary Algorithm (EA) to evolve high accuracy classifiers that differentiate Parkinson's disease patients from healthy controls (Lones et al. 2012) (Smith and Timmis 2008). Further investigation into classifiers evolved was able to characterise movement disorder in PD (Lacy et al. 2013) and inform clinical assessment (Lones et al. 2013). Based on the success of using FT data, we believe that EAs can also be used on other motor tasks to achieve the same if not better results. Specifically, this study extends our work to other common clinical motor tasks; pronation-supination (PS) and hand opening-closing (OC) tasks. FT was also included in this study for validation and comparison purposes.

Cartesian Genetic Programming (CGP), a type of EA was used to train classifiers. CGP was introduced by Miller and Thomson (Miller and Thomson n.d.) where the candidate solutions are represented as a string of integers of fixed length that is mapped to a non-cyclic directed graph. CGP and its variants have shown excellent ability in the classification of a range of medical applications including the classification of mammograms for the detection of breast cancer (Hope et al. 2007) and diagnosis of Alzheimer's disease (Hazell and Smith 2008). Additionally, there were also classifications using bio-signals such as spectral data for evaluation of cancerous thyroid cell lines (Lones et al. 2010), digital images of the cells to differentiate benign and malignant breast mass cells (Ahmad et al. 2012) and electrocardiography (ECG) signals to classify cardiac arrhythmia types (Ahmad et al. 2013).

A distinct advantage of EAs is that the classifiers evolved can be scrutinised to discover which features, or even, which parts of the movement data were used in their construction. Although statistical machine learning methods such as SVM usually able to generate comparable classifiers, it requires extra steps to identify most discriminating inputs. A technique such as forward-selection wrapper approach or other feature ranking methods had to be integrated to achieve the same objective.

The main objectives of this paper are to look into the potential of applying EAs to evolve classifiers using movement data of PS and HO tasks and evaluate possible Bradykinesia characteristics that later can be used to inform clinical assessments.

2 METHODOLOGY

After obtaining informed written consent, 20 controls and 22 patients with idiopathic Parkinson's disease were tested using the Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) in a conventional clinical setting at the Monash Medical Centre, Melbourne, Australia. The finger tapping, pronation-supination and hand opening-closing components of the MDS-UPDRS were assessed both clinically and using an objective motion tracking system.

2.1 Movement Data Collection

The motion tracking system used for movement recording employ Polhemus Patriot Electromagnetic (EM) tracking sensors (Polhemus 2016). The system consists of electronic system unit (SEU), a magnetic transmitter and two EM tracking sensors. Each participant wears the EM sensors on index finger and thumb when they perform the specified assessments. The EM sensors record position and orientation relative to the transmitter in six degrees of freedom with an update rate of 60 Hz per sensor. The system returns three Cartesian coordinates (X, Y, and Z) and three orientation Euler Angles: azimuth, elevation and roll.

2.2 Movement Features

Features were extracted based on the current clinical definition of bradykinesia and the nature of the movement in each task.

2.2.1 Finger Tapping

In this study, patients were asked to perform the standard clinical finger tapping test as defined by the Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS). This instructs patients to perform ten finger taps as fast and as wide as possible. As one of the final objectives of this study is to inform clinical assessment, it is important for the

task to be performed identically with standard clinical evaluation.

The separation **distance** between the finger and the thumb during the finger tapping action was computed by first calculating the difference between the x, y and z coordinate values for the respective sensors, and then, the Euclidean distance, or overall positional separation, between index finger and thumb. **Speed** and **acceleration** were calculated as the first and second derivatives of the distance, respectively. The raw movement data was also preprocessed to remove noise using Low Pass 5Hz Butterworth filter. Butterworth filter is most common filter used in biomechanics data analysis due to its excellent passband response (Christodoulakis et al. 2010).

Patients often have difficulties in performing the exact number of the cycles as instructed. Therefore, **cycles frequency** is one of the features selected instead of time taken to finish the task. Other features were quantified for the opening and closing phases of the cycle. The opening phase begins once the fingers are separated, from an initially closed position – equating to a minimal distance between the sensors – to when they are maximally separated; the closing phase begins once the sensors move towards one another after the point of maximal separation and finishes when the sensors have achieved a minimum separation.

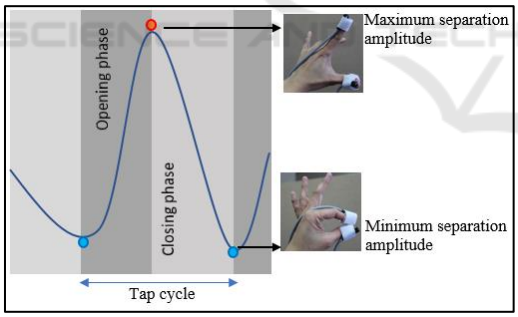

Figure 2: Separation data showing opening and closing phases of a tapping cycle.

Figure 2 provides a representation of positional separation data, showing opening and closing phases of a cycle. Minimum, maximum and average of normalised speed and acceleration of both cycle phases were computed according to (Lacy et al. 2013). To measure rhythm, Coefficient of Variation (COV) was used. **COV** reflects how much a movement component measure varies over a defined period. It may be considered a measure of how rhythmic the repetitive movements are. COV of amplitude was calculated over a period of tapping cycles as follows:

$$COV\ speed = \frac{\sigma\ cycles\ max\ speed}{\mu\ cycles\ max\ speed} \quad (1)$$

To calculate the **decrementing trend**, maximum separation amplitude or speed for each tap cycle was linearly regressed against the number of cycles. A negative slope indicates that the overall trend of a movement component measure is decrementing and a zero or positive slope indicates that the amplitude is not decrementing. Figure 3 provides examples of linear regression plots of maximum amplitude to obtain the slope indicating a trend of separation amplitude. Measures of amplitude and speed alone may not have captured the real movement patterns of subjects. To capture the relationship between these components a variable called **periodicity** was calculated.

$$Periodicity = max\ amplitude \times max\ speed \quad (2)$$

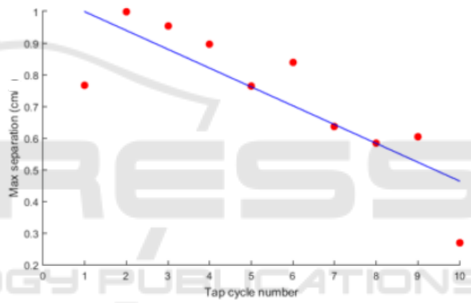

Figure 3: An example of tap decrementing trend for a patient with slope = -0.6.

Other features extracted are **halts**, **hesitation** and **amp*freq**. Halts were measured by calculating the percentage of the tap cycle duration spent at 'zero' (< 5% of the maximum) speed:

$$Halts = \frac{Time\ < 5\%\ max\ speed}{time\ taken\ (task)} \times 100\% \quad (3)$$

When the movement showed smaller peaks between tapping cycle phases (Figure 4), it is treated as hesitation**.**

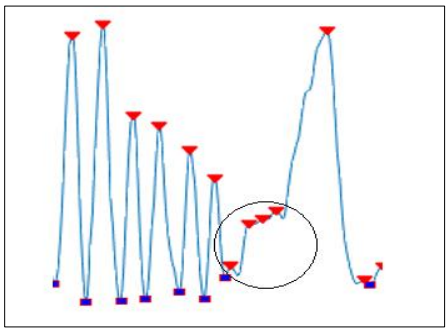

Figure 4: The smaller peaks counted as four hesitations.

Bigger amplitude with greater frequency during finger tapping means faster finger movement. This is considered as better performance. Alternatively, the movement can be executed faster with smaller amplitude. The amplitude × frequency of tapping is suggested in (Jobbágy et al. 2005) to characterise the speed. This feature is determined for each tapping cycle and then averaged over the whole test. Table 1 summarises all features used as inputs to the CGP classifier.

Table 1: Finger tapping extracted features.

	Feature
(0)	Cycles frequency
(1)	Max overall amplitude
(2)	Mean amplitude
(3)	Maximum overall speed
(4)	Max opening speed
(6)	Max closing speed
(7)	Max opening acceleration
(8)	Max opening deceleration
(9)	Max closing acceleration
(10)	Max closing deceleration
(11)	Periodicity
(12)	COV amplitude
(13)	COV speed
(14)	Decrementing amplitude
(15)	Decrementing speed
(16)	Halts
(17)	Hesitation
(18)	Amp*freq

2.2.2 Hand Pronation-supination

For the hand pronation-supination task (PS), the MDS-UPDRS requires the participant to extend the arm out in front of their body with the palms face down and then turn the palm up and down alternately 10 times as fast and fully as possible.

After some experimentation, it was concluded that the most useful data in our pronation-supination recordings came from the movement of the thumb. Since only one sensor is used, the **amplitude** is defined as the Euclidean distance between thumb sensor and Patriot transmitter.

$$amp\ (t) = \sqrt{x(t)^2\ +\ y(t)^2\ +z(t)^2} \quad (4)$$

Velocity was calculated by differentiation of each Cartesian coordinate component (x, y, z) over the sampling time period to compute the respective velocity components ($v_{x,}v_{y,}v_z$). The total velocity was computed from the sum of its components and its magnitude, the **speed**

$$vel(t) = \sqrt{v_x(t)^2\ +\ v_y(t)^2\ +v_z(t)^2} \quad (5)$$

Acceleration is obtained by differentiating the velocity, using the same sampling time. The same features in Table 1 were used for PS classifiers by replacing opening and closing phases with pronation and supination phases respectively.

Since PS involves angular movements, movements were computed using Euler angles. Average, minimum and maximum of **angular velocity** and **angular acceleration** values were calculated according to (Picardi et al. 2010), giving the additional six angular features shown in Table 2.

Table 2**:** Hand pronation-supination features.

	Feature
(19)	Mean angular speed
(20)	Max angular speed
(21)	Min angular speed
(22)	Mean angular acceleration
(23)	Max angular acceleration
(24)	Min angular acceleration

2.2.3 Hand Opening-closing

For the hand opening-closing task (HO), the MDS-UPDRS requires the participant to make a tight fist with the arm bent at the elbow so that the palm faces the examiner and then requires the participant to open the hand ten times as fully and as quickly as possible. Sensors were placed at the same positions as in finger tapping task. However, unlike finger tapping, which is a simultaneous movement of thumb and fingers, the hand-opening task involves two steps movements. Therefore, the features extracted were also taking into account the measurements of both sensors separately, instead of just considering the distance between the two sensors. The thumb sensor (TS) and finger sensor (FS) movement data were used to compute the total of seventeen features. (Table 3).

Table 3: Hand opening-closing extracted features.

	Feature
(0)	HO frequency
(1)	Maximum opening
(2)	COV opening
(3)	TS average speed
(4)	TS minimum speed
(5)	TS maximum speed
(6)	TS minimum acceleration
(7)	TS maximum acceleration
(8)	TS COV speed
(9)	TS Halts
(10)	FS average speed
(11)	FS minimum speed
(12)	FS maximum speed
(13)	FS minimum acceleration
(14)	FS maximum acceleration
(15)	FS COV speed
(16)	FS Halts

2.3 Classification

Classification used a typical CGP evolutionary strategy which selects one parent from each generation and uses mutation to produce four children. The next generation then comprises the parent and the four children, giving a population of size five - four children plus one parent: (1+4) - ES. Three sets of classifiers were evolved, one for each movement task. The input data consists of floating point values representing selected Bradykinesia features extracted from the patient's movement (as defined in section 2.2).

The fitness assigned to each classifier is simply the proportion of samples correctly classified. Previous CGP classifiers in FT studies (mentioned in the introduction) used the area under a ROC Curve (Fawcett 2006) as fitness function, but in this study, classification accuracy is used for simplicity and direct comparison. Through experimentation, the following CGP parameters values were adopted: number of nodes available 15, nodes arities of 2, mutation rate of 0.05 and number of generations 10000. The function set comprised ($\{+, -, \times, \div, mean, min, \max, mode\}$). Data from each class was divided into training and test sets. To compensate for any effect on results caused by small amounts of training and test data, 5-fold cross validation was used. Results are averaged over ten runs for statistical significance. The best classifier model is used to determine those features that are most discriminative.

3 RESULTS

With numbers of subjects relatively low compared to our previous FT studies, the classifications accuracies in this study are surprisingly good. For the finger tapping task, averaged accuracy of the test set across ten runs is 82.66%. For the pronation-supination task, 80.54%, and for the hand opening task, 75.32%. Best and average accuracies of all tasks are summarised in table 4.

Table 4: Average and best accuracies of classifiers evolved for all motor tasks.

Task	Accuracy			
	Averaged ten runs		Best run	
	train	test	train	test
FT	91.69	83.3	91.79	87.20
PS	92.04	80.54	94.34	84.03
HO	92.92	75.32	94.27	80.21

Figure 5 showing the distribution of cross-validated classification accuracies for ten runs of each task.

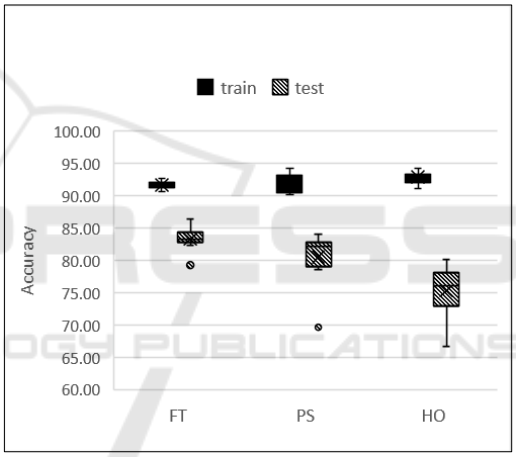

Figure 5: Distribution of accuracies across ten runs.

As mentioned in the introduction, one of the main advantages of using GP method is the ability to recognise which inputs were used to evolve the strongest classifier. For example, the PS classifier with 85% accuracy is visualised in figure 6, showing only the active nodes.

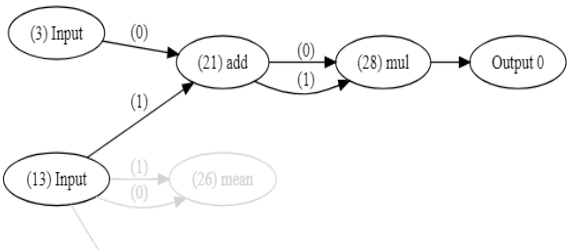

Figure 6: Visualisation of a PS classifier.

In this example, the inputs used are maximum

overall speed and speed rhythm (COV). All features used to evolve the best classifier of each task are summarised in table 5.

Table 5: Most discriminating features for each task.

Task	Features
FT	(4)(7)(9) (14) from Table 1
HO	(0)(2)(3)(4)(5)(6) (14) from Table 2
PS	(8) (13) (14) (16) (17) (20) from Table 1* and Table 2

** replaced opening phase with pronation phase and closing phase with supination phase.*

4 CONCLUSIONS

It is clear from the classification results that hand opening-closing and hand pronation-supination have the same potential as finger tapping to be used as a tool in the characterisation of Bradykinesia using GP to inform clinical assessment. The overall accuracy was lower than shown in previous studies of GP classifications using finger tapping data, but we believe this is due to smaller numbers of subjects. Almost all classifiers across ten runs for all tasks are consistent with good accuracies above 70%. Although the most discriminative movement features in this study may not be generalised to inform clinical assessment because of the small sample numbers, it was demonstrated that by using GP, it could easily be acquired.

Movement features are computed based on the current clinical definition of Bradykinesia. However, CGP has the ability to accept raw positional or speed data points and perform an unbiased search that will not be constrained by pre-defined characteristics. Future work will process PS and HO data using a sliding window, similar to FT acceleration data in continuous time series adopted by (Lones et al. 2014). By using raw data points to induce classifiers, it opens the possibility of finding new features of Bradykinesia from the movement tasks.

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