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Objective evaluation of bradykinesia in Parkinson's disease using an inexpensive marker-less motion tracking system

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Objective Evaluation of Bradykinesia in Parkinson's Disease using an Inexpensive Marker-less Motion Tracking System

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Abstract

Objective: Quantification of bradykinesia (slowness of movement) is crucial for the treatment and monitoring of Parkinson's disease. Subjective observational techniques are the de-facto 'gold standard', but such clinical rating scales suffer from poor sensitivity and inter-rater variability. Although various technologies have been developed for assessing bradykinesia in recent years, most still require considerable expertise and effort to operate. Here we present a novel method to utilize an inexpensive off-the-shelf hand-tracker (Leap Motion) to quantify bradykinesia.

Approach: Eight participants with Parkinson's disease receiving benefit from deep brain stimulation were recruited for the study. Participants were assessed "on" and "off" stimulation, with the "on" condition repeated to evaluate reliability. Participants performed wrist pronation/supination, hand open/close, and finger-tapping tasks during each condition. Tasks were simultaneously captured by our software and rated by three clinicians. A linear regression model was developed to predict clinical scores and its performance was assessed with leave-one-out cross validation.

Main Results: Aggregate bradykinesia scores predicted by our method were in strong agreement (R = 0.86) with clinical scores. The model was able to differentiate therapeutic states and comparison between the test-retest conditions yielded no significant difference (p = 0.50).

Significance: These findings demonstrate that our method can objectively quantify bradykinesia in agreement with clinical observation and provide reliable measurements over time. The hardware is readily accessible, requiring only a modest computer and our software to perform assessments, thus making it suitable for both clinic- and home-based symptom tracking.

Keywords: Bradykinesia, Leap Motion, Motion Capture, MDS-UPDRS, Parkinson's Disease

1. Introduction

Parkinson's disease (PD) is a neurological disorder that affects approximately 1% of the population over the age of 60 in the United States (DeMaagd and Philip 2015). Patients suffer from a progressive reduction in mobility and muscle control leading to an inability to perform routine tasks such as walking and dressing. Bradykinesia is a cardinal symptom of PD and is often a core disabling symptom alongside tremor and rigidity (Goldenberg 2008). This is typically characterized by the progressive loss of amplitude and speed when rapid alternating movements are attempted (Jankovic 2008). Accurate assessment of bradykinesia is crucial for managing PD. The variability of disease progression among patients leads to frequent therapeutic adjustments requiring clinical assessment to determine efficacy.

The Movement Disorder Society's Unified Parkinson Disease Rating Scale (MDS-UPDRS) (Goetz *et al* 2008) is widely used by clinicians to assess symptoms including bradykinesia. This rating scale requires the patient to perform a series of repetitive movement tasks which are observed by the clinician and rated between 0 (normal) and 4 (severe) to indicate impairment. Such clinical rating scales have several disadvantages: 1) insufficient sensitivity to detect minor variations due to integer-based scoring, 2) a suitably qualified clinician is required to administer the assessment leading to inter-rater variability (Richards et al 1994, Post et al 2005), and 3) intra-day symptom fluctuations cannot be captured to guide therapy. Furthermore, patients residing in remote communities lack access to specialist clinics leading to a growing demand for objective monitoring systems that can be deployed in the absence of a movement disorders expert. Therefore, there is a growing requirement to introduce technologies that can quantify each patient's symptoms objectively and reliably across multiple time-points without the presence of an expert clinician (Odin *et al* 2018, Rovini *et al* 2017, Espay *et al* 2016).

To date, several technologies have been proposed for bradykinesia assessment, each with its own limitations. Technologies such as electromagnetic tracking systems (Espay *et al* 2009, Perera *et al* 2016) and marker-based motion capture systems (Smeragliuolo *et al* 2016, Galna *et al* 2014) can provide precise analysis of movement. However, they are expensive and difficult to operate, and require a dedicated space where devices are often placed in fixed positions. Meanwhile, technology such as quantitative digitography can evaluate patients based on a simple keyboard-tapping task (Taylor Tavares *et al* 2005). Other technologies that employ wearable motion sensors (Dai *et al* 2015, Delrobaei *et al* 2016, Stamatakis *et al* 2013, Kim *et al* 2011, Salarian *et al* 2007) are promising and have shown varying degrees of success in measuring bradykinesia (Hasan *et al* 2017). Yet, the majority of these published studies used motion sensors for evaluating a single circumscribed movement task (Martinez-Manzanera *et al* 2016, Kim *et al* 2011, Stamatakis *et al* 2013, Mera *et al* 2012, Heldman *et al* 2011, Giuffrida *et al* 2009, Rovini *et al* 2014). It is challenging to evaluate multiple tasks using a single motion sensor, and the concept of multiple body-worn sensors increases setup complexity, is prohibitively time-consuming, and increases the likelihood of error (Delrobaei *et al* 2016, Rovini *et al* 2014, Noort *et al* 2017).

Despite the promising results from technology-based rating tools, MDS-UPDRS remains the gold standard in bradykinesia assessment (Maetzler *et al* 2013, Pal and Goetz 2013). Objective instruments are yet to be widely incorporated into routine clinical evaluation for several reasons. Firstly, the practicality of a device is important because bulky, expensive, and complicated devices inhibit clinical adoption (Pal and Goetz 2013). Secondly, a reasonable correlation between an objective measurement and widely-accepted clinical scales must be achieved to demonstrate its validity (Odin *et al* 2018, Rovini *et al* 2017). Lastly, although an objective measurement could potentially measure bradykinesia severity beyond the existing rating scale, the measured values may not be easily understood. Therefore, an alternate strategy that could increase clinician adoption is to determine a transformation between the existing rating scale and the objective rating tools. An example approach is to identify the sensor-based features that are relevant to PD symptoms and map them onto the existing clinical scales (Giuffrida *et al* 2009, Pulliam *et al* 2014).

The Leap Motion Controller (Leap Motion, San Francisco, USA) is a consumer-gaming device that can estimate human hand movements in three-dimensional space without the need for wearable sensors or markers. This device can provide a reliable measurement and has good overall agreement (R = 0.79 to 0.95, RMSE = 11.6° to 38.4°) with marker-based motion-capture systems (Smeragliuolo *et al* 2016). Its remote hand-tracking capability has also led to its use in applications such as sign-language interpretation (Chuan *et al* 2014), motor rehabilitation (Oña *et al* 2018), and tremor quantification (Chen *et al* 2016). Recently, Butt *et al* 2017 also demonstrated the potential of using this device to differentiate healthy and PD patients. Specifically, their goal was to classify bradykinesia assessments as either normal (healthy) or abnormal (PD). Classification algorithms were trained using 17 kinematic features extracted from Leap Motion data in 16 PD and 12 healthy participants.

Despite achieving sensitivity and specificity of approximately 80%, a key question remains unanswered: can Leap Motion be used to quantify the level of bradykinesia severity within the PD population?

In the study reported below, we aimed to quantify the overall bradykinesia severity in PD using a Leap Motion Controller. Moreover, we sought to determine if a multitude of hand tasks are required, or if just one is sufficient to characterise symptom severity. We hypothesized that the Leap Motion Controller can objectively determine the MDS-UPDRS score with reasonable accuracy, acceptable test-retest reliability, and that a combination of tasks would yield the best prediction.

2. Methods

2.1 Participants

Eight participants (aged 44-60 years, 6 male) with levodopa-responsive PD (mean disease duration: 10.3 ± 3.8 years) receiving chronic bilateral subthalamic nucleus deep brain stimulation (DBS) therapy for six months or longer were recruited. Exclusion criteria included: 1) inability to participate off-medication, 2) known or suspected bone disease (osteoporosis, rickets, etc.), 3) known or suspected joint disorders (arthritis, bursitis, gout, etc.), and 4) chronic neuromuscular disorders (e.g. muscular dystrophy). Participants arrived on-DBS, off-medication (after a minimum of 12 hours withdrawal of medications), and gave written informed consent. No medication was given during the study. The study was approved by the Human Research Ethics Committee of St Vincent's Hospital, Melbourne (HREC/16/SVHM/32).

2.2 Leap Motion Controller

The Leap Motion Controller is a portable USB device that utilizes miniature infrared cameras and inbuilt image recognition algorithms to identify and estimate hand positions in three-dimensional space (Figure 1a,b) (Colgan 2014). A software development kit (version 2.3.1), available from the manufacturer, enables custom software to acquire hand joint positions at a variable sampling rate centred around 120 Hz. The device is ideally suited for desktop use, but can be mounted on a small tripod to give greater flexibility. The tracking range extends from 2.5 to 60 cm above the device, with field-of-view of 150˚ horizontally and 120˚ vertically. The Leap Motion Controller is affordable; at the time of writing, it was available through the manufacturer's website for USD $80.

2.3 Assessment Protocol

Wrist pronation/supination, hand-open/close, and finger-tapping motor tasks in accordance with MDS-UPDRS were used in this study (Goetz *et al* 2008). During the experiment, participants performed these tasks sequentially while being concurrently monitored by the Leap Motion Controller and three expert clinicians, a Parkinson's disease nurse (MJ) and two physiotherapists experienced in the management of Parkinson's disease (JLT, ELP). The clinicians were blinded to the experimental protocol. To prevent bias, clinicians were instructed not to verbalize their ratings.

The Leap Motion Controller was rested flat on a table in front of the participant and the computer screen was hidden from view. Under the instruction of a clinician (JLT), participants performed tasks by consecutively placing each hand over the Leap Motion Controller. At least 10 repetitions of each task were captured. All clinicians simultaneously rated each task according to the scale provided in the MDS-UPDRS.

The average clinical score across all tasks (maximum possible score of 4) was used as a measure for the overall bradykinesia severity. All tasks were assessed under different therapeutic conditions: 1) DBS-$ON_{baseline}$: beginning of the study while receiving DBS therapy; 2) DBS-OFF: 60 mins following DBS cessation; and 3) DBS-ON_{post}: 30 mins following DBS therapy resumption.

2.4 Data Processing

The Leap Motion Controller provides time-series position and orientation data for joints within the hand. Custom C# software was developed in-house to record the raw data (Figure 1a). The software interface allowed the user to begin and end recording as well as input trial conditions. Time-stamped data were analysed off-line using MATLAB v2017a (Mathworks Inc., Natick, MA) after completion of the study.

Leap Motion data were reconstructed to obtain kinematic signals that describe each task (Figure 1c,d,e). Angular displacements of the palm in the roll axis were generated for the pronation/supination exercise. The grip angle (median cosine angle between palm and intermediate phalanges of all fingers) quantified the hand open/close task. Lastly, Euclidean distance between the tip of the thumb and index finger provided a metric for finger-tapping.

As the Leap Motion Controller acquired samples at a variable rate, and only returned data whenever a hand was successfully detected, we resampled the kinematic signals to 120 Hz using a linear interpolation method, but discarded any segment which was interpolated over a blank period of greater than 0.5s. The signals were de-trended, movement initiation and cessation were identified by thresholding, and only data within the defined movement period was used for subsequent processing (Figure 2a,b,c).

Figure 1 – Custom software (a) developed in C# for acquiring hand position using the Leap Motion Controller (b). The software provides real-time rendering of the hand positions and allows assessments to be recorded effortlessly. Time-series kinematics extracted from the Leap Motion Controller for quantifying hand exercises include: (c) roll angle for pronation supination, (d) grip angle for hand open/close tasks, and (e) tapping distance for finger-tapping movements.

2.5 Feature Generation

Amplitude, frequency, velocity, slope, and variance were extracted from each movement to represent the kinematic features of bradykinesia. Firstly, the positive and negative peaks of a signal were identified by finding the local maxima and minima above/below the zero-crossing point respectively. The movement frequency was computed as the inverse of the mean peak-to-peak time interval. The positive and negative envelopes of a signal were constructed by interpolating the positive and negative peaks respectively (Figure 2d). The movement amplitude was computed as the mean envelope difference. By time-differentiating the kinematic signal, the movement velocity was computed as the mean absolute velocity. The slope of each movement was computed as the gradient of the linear regression applied to the amplitude signal. Finally, the variance of each movement was computed as the variance of the amplitude signal after de-trending by the linear regression gradient.

2.6 Regression Model

Clinical ratings were averaged to reduce inter-rater variability. The average rating, which was continuous after averaging, was used as the "ground-truth" training data. A standard linear least-square regression technique was applied to correlate the kinematic features with the overall bradykinesia severity score (average MDS-UPDRS ratings across tasks), with the assumption of normal error distribution in transformation between kinematic features and clinician MDS-UPDRS ratings. The leave-one-subject-out cross-validation (LOSOCV) method was employed to examine the performance of each regression model against unseen data, as well as to reduce bias in the evaluation due to within-subject repeated measures. All the predicted scores were bound within the range between 0 and 4.

The best feature combination (having the highest correlation with clinical ratings) was identified by testing all possible combinations using LOSOCV (exhaustive search of 32,767 feature combinations). Specifically, the samples from all subjects except one were selected for model training, while samples from the excluded subject were used for model testing. The process of model training and testing was repeated until samples from all available subjects were tested. The performance of each feature combination was assessed by computing the correlation coefficient (R_{cv}) and Root-Mean-Square Error ($RMSE_{cv}$) between the predicted scores and the clinical rating. If the best performing model combined features from more than one task, results from the exhaustive search were filtered to systematically exclude each task, thus providing a basis for comparing the contribution of each task to the cumulative model performance.

2.7 Reliability of Clinician and Predicted scores

The reliability of the clinical scores was evaluated using the intra-class correlation (ICC) method using a two-way absolute-agreement random-effect model (Koo and Li 2016). $ICC_{2,1}$ computed the reliability of a single clinician against others, and $ICC_{2,3}$ computed the reliability of the mean clinical score. Test-retest reliability for both the clinical and predicted scores was assessed using a non-parametric repeated measures Friedman's test and post-hoc Wilcoxon signed rank test in MATLAB.

3. Results

A total of 144 trials were recorded (8 subjects x 2 hands x 3 therapeutic conditions x 3 tasks). Each trial comprised three independent MDS-UPDRS clinical ratings matched to the corresponding Leap Motion data. The median trial duration was 11.7 s (interquartile range: 9.3 to 14.0 s). Missing data was apparent in 14 trials with the Leap Motion Controller failing to detect the hand for a period greater than 0.5 s. In each case, the hand was positioned above the sensor and the participant was performing a task, indicating a failure of the Leap Motion Controller to detect the hand. Seven of the affected trials occurred during the wrist pronation/supination task. The median percentage of missing data within the affected trials was 13.5% (interquartile range: 9.0% to 25.8%). These trials were not excluded from the analysis despite gaps in acquisition.

An exhaustive LOSOCV assessment identified wrist pronation/supination, hand open/close, and finger-tapping as the best task combination for predicting the overall bradykinesia severity (R_{cv} = 0.86, $RMSE_{cv}$ = 0.45, Table 1). Correlations and RMSE remained comparable when the feature set was reduced to only represent pronation/supination and hand open/close tasks. Individual tasks only yielded moderate correlations with finger-tapping performing worst. Interestingly, of the 15 features included in the exhaustive search, including the slope and variance measures, only a few were significant. For the wrist pronation/supination task, amplitude of the movement best correlated with clinical ratings. Similarly, velocity alone was best for the hand open/close task. Finger-tapping exploited both velocity and frequency, yet gave poor correlations with ratings.

Mean clinical scores had greater reliability ($ICC_{2,3}$ = 0.86) compared with single clinical scores ($ICC_{2,1}$ = 0.68), suggesting that the mean clinical scores collected in this study were reliable and more suitable than single clinical scores for training the linear regression model. Both the clinical (D = 0.748, $p < 0.001$) and predicted bradykinesia ratings (D = 0.729, $p < 0.001$) were non-normally distributed under the one-sample Kolmogorov–Smirnov test. Thus, Friedman's test, a non-parametric repeated-measures comparison test, was selected for evaluating the test-retest reliability. Differences between therapeutic conditions were found in both the clinical ratings ($\chi^2(2) = 15.77$, $p < 0.001$) and the predicted bradykinesia scores using all three tasks ($\chi^2(2) = 7.63$, $p = 0.022$). Post-hoc comparisons revealed significant differences (Figure 3) between $DBS\text{-}ON_{baseline}$ and DBS-OFF for both clinical (Z = -3.47, $p < 0.001$) and predicted (Z = -3.05, $p = 0.002$) scores. Differences were also seen

between DBS-OFF and DBS-ON$_{post}$ in both clinical (Z = 2.90, p = 0.004) and predicted scores (Z = 2.22, p = 0.026). No significant differences were evident between the DBS-ON$_{baseline}$ and DBS-ON$_{post}$ for both clinical (Z = 0.000, p = 1.000) and predicted scores (Z = -0.67, p = 0.500).

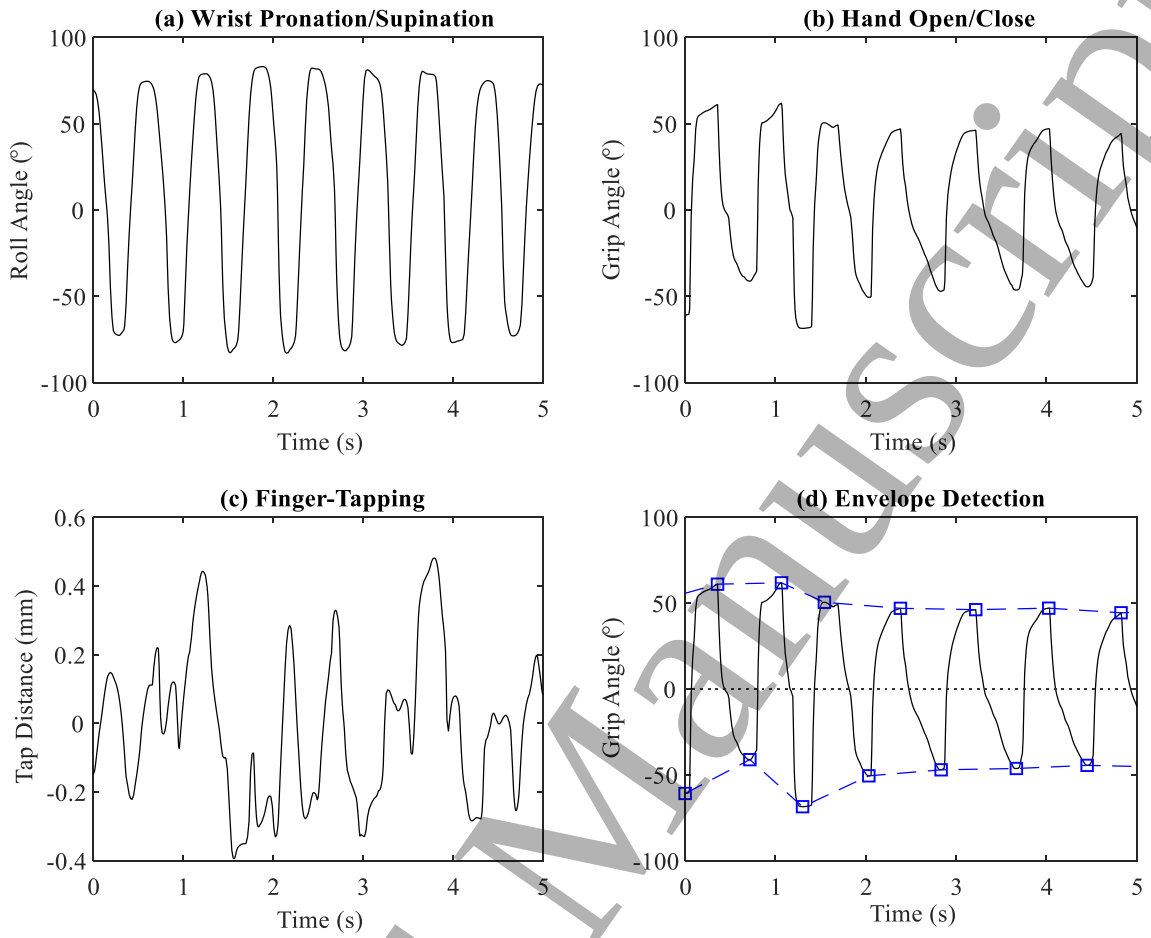

Figure 2 – Representative segment of the kinematic signal reconstructed from (a) wrist pronation/supination, (b) hand open/close, and (c) finger-tapping tasks. The envelope detection for the hand open/close exercise is shown in (d).

Table 1 – The correlation coefficient (R_{cv}) and Root-Mean-Square Error (RMSE$_{cv}$) between the mean clinician ratings and the predicted ratings when the best feature combination from the exhaustive search was filtered by task. PS = Wrist Pronation/Supination; OC = Hand Open/Close; FT = Finger-tapping. * denotes the best feature combination identified by cross validation.

Tasks	Features	R_{cv}	RMSE$_{cv}$
FT	FT-velocity, FT-frequency	0.45	0.81
PS	PS-amplitude	0.56	0.74
OC	OC-velocity	0.69	0.65
OC & FT	OC-velocity, FT-velocity, FT-frequency	0.70	0.65
PS & FT	PS-amplitude, FT-velocity, FT-frequency	0.71	0.64
PS & OC	PS-amplitude, OC-velocity	0.85	0.47
PS, OC & FT*	PS-amplitude, OC-velocity, FT-velocity, FT-frequency	0.86	0.45
PS, OC & FT	All Features	0.77	0.61

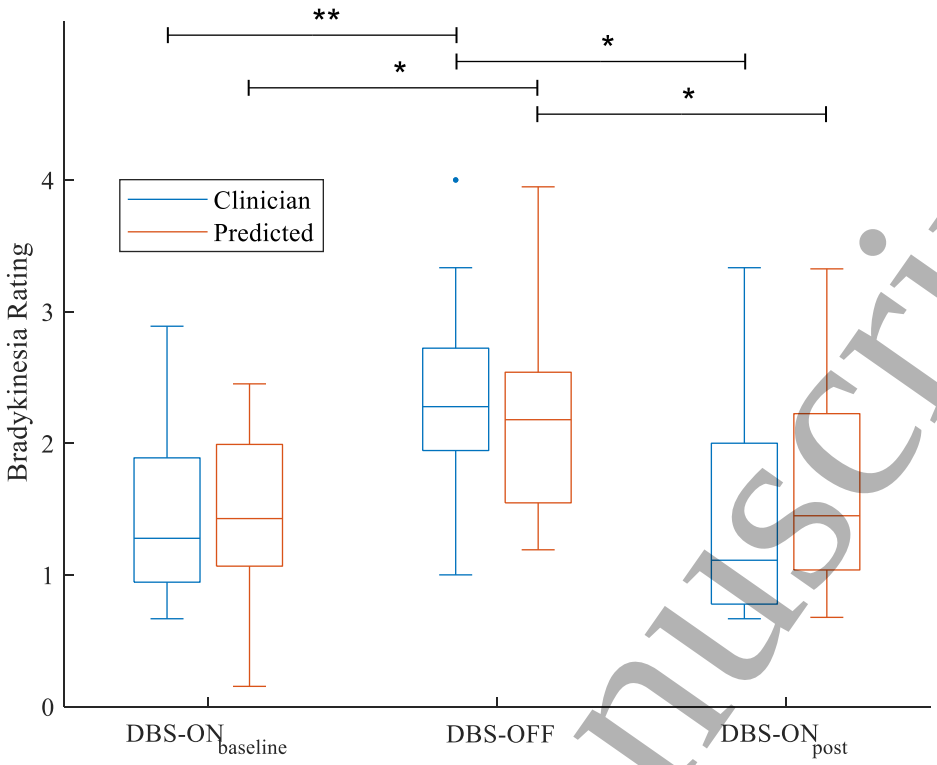

Figure 3 – The overall bradykinesia ratings across different therapeutic conditions as denoted by clinicians and predicted by our software using all three tasks. Boxplot: centre line = median; top bar = 75th percentile; bottom bar = 25th percentile; whiskers indicate minimum and maximum; outliers (outside the 1.5 interquartile range) marked with dots. * = $p < 0.05$; ** = $p < 0.001$; paired Wilcoxon signed rank test.

4. Discussion

We developed a novel method to quantify bradykinesia severity in PD using the Leap Motion Controller. Using regression modelling and careful selection of kinematic features, our results demonstrate that data obtained from the Leap Motion Controller can predict the overall bradykinesia severity in agreement with clinical observation and provide reliable measurements over time. Moreover, our results indicate that the inclusion of the finger-tapping task yielded no substantial improvement to bradykinesia predictive performance, likely due to finger tracking inaccuracies.

Predicted bradykinesia ratings had high congruence with clinical MDS-UPDRS ratings, suggesting the extracted kinematic features can explain the variation in bradykinesia severity. Our results support the finding by Heldman *et al* 2011 that amplitude, frequency, and velocity were crucial for assessing bradykinesia severity. Yet, unlike others (Stamatakis *et al* 2013, Martinez-Manzanera *et al* 2016, Kim *et al* 2011, Heldman *et al* 2011), we found finger tapping did not add significant predictive power to our model. Furthermore, we obtained a reliable prediction without the variance and slope features described by Ling *et al* 2012. In our experience, the Leap Motion Controller is prone to error when tracking finger movement. Figure 2c shows indicative raw data where the finger-tapping amplitude is unexpectedly within the sub-millimetre range. The Leap Motion Controller often fails to track fingers during tapping and as such could have compromised the extracted features. Nevertheless, we were able to obtain a model congruent with clinical ratings with wrist pronation/supination and hand open/close tasks. Although the level of prediction improvement with an accurately-tracked tapping task remains uncertain, our model is comparable to existing methods. Notably, Rovini *et al* 2014 deduced a regression model with high agreement ($R = 0.87$) between clinical MDS-UPDRS bradykinesia ratings and multiple inertial sensors placed on the hand. Taylor Tavares *et al* 2005, using quantitative digitography, also reported that repetitive keyboard-tapping tasks were moderately congruent ($R = 0.704$) with clinical assessments (UPDRS).

Feature reduction not only reduces the computational complexity of the model, but also has important clinical relevance. If a subset of hand tasks can characterise bradykinesia, then it offers a time-saving benefit. Our results indicate that bradykinesia severity can be deduced without finger-tapping. In terms of duration, our technique took on average 23.4 s to complete two tasks prior to bradykinesia estimation. The assessment duration is reasonable and comparable to other existing devices that require 30 s in their assessment (Rovini *et al* 2014, Taylor Tavares *et al* 2005).

The predicted bradykinesia ratings obtained by combining all three tasks differentiated therapeutic states corresponding to DBS on and off. Furthermore, no statistically significant difference was seen between the DBS-ON$_{baseline}$ and DBS-ON$_{post}$ conditions which were expected to be therapeutically equivalent. The results suggest that the prediction model produces a consistent and reliable score, which supports its use in clinical assessments. Importantly, we used averaged ratings from three independent clinicians to train our regression model in order to reduce inter-rater variability. In practice, it is often infeasible to obtain ratings from multiple clinicians during routine assessments and clinical trials. An objective assessment tool, such as the one proposed here, is therefore advantageous and may not only improve patient care, but also the accuracy and reliability of symptom severity reported in clinical trials.

The Leap Motion Controller coupled with our model enables higher measurement resolution on a continuous scale, thus allowing greater sensitivity in monitoring bradykinesia than clinical ratings. Given that our method also predicts bradykinesia severity in a 0 to 4 range, the results can be easily interpreted using MDS-UPDRS definitions and translated to effect on patient quality-of-life. Considering practicality, the Leap Motion Controller can monitor hand motion without any sensors or markers placed on the participant's hands. This avoids complications associated with sensor placement and calibration often required with other methods (Iosa *et al* 2016). It also allows patients freedom of movement given the passive nature of data collection unimpeded by wired body-worn sensors. Hand detection is a fundamental feature of the Leap Motion Controller and it will automatically begin and end recording according to the presence or absence of hands. Thus, participants can easily move between various clinical assessments or other activities interleaved with bradykinesia monitoring. Finally, in contrast to existing techniques, the raw data recorded from the Leap Motion Controller is meaningful and can be readily rendered to allow visualization of the hand motion, thus aiding interpretation of the results and perhaps leading the way to remote monitoring solutions for telehealth.

Despite the positive outcomes reported above from the use of the Leap Motion Controller, several tracking issues with the device should be mentioned. In this study, the participants were allowed to perform hand movements naturally without any restriction, other than facing their palm towards the Leap Motion Controller. Our experience suggests that the Leap Motion Controller is functionally reliable, with only a small number of trials suffering from missing data. Momentary loss of tracking is most evident when the fingers are occluded, for instance where the roll or elevation of the hand is perpendicular to the sensor. Furthermore, the device's automatic hand-orientation algorithm has a tendency to misclassify the hand (left or right) during wrist pronation/supination when the hand moves between angles which cause transition from palm-down to palm-up. Despite accurately tracking the hand pose, estimating the finger position at millimetre resolution remains a challenge not only for the Leap Motion Controller, but also for most existing image-based hand-tracking devices (Qian *et al* 2014).

Several measures could be implemented in the future to mitigate the tracking issues in the Leap Motion Controller: 1) an arm rest could be provided to ensure participants maintain consistent posture and distance when performing exercises; 2) the automatic hand-side detection algorithm should be disabled to prevent left/right switching during continuous tracking; and at the risk of increasing complexity, 3) additional Leap Motion Controllers to monitor hand movements from different perspectives can be used to improve data quality (Jin *et al* 2016). Moreover, the hand-tracking algorithm could be improved by either using the latest manufacturer updates or implementing custom tracking algorithms (Sharp *et al* 2015).

Limitations of our proof-of-concept study must be acknowledged. First, it should be highlighted that although we attempted to collect samples with varying degrees of bradykinesia scores, it was challenging to recruit subjects with severe bradykinesia. Therefore, the small sample size and uneven distribution of clinician ratings may prohibit robust generalization of our model. Second, we did not ascertain the minimum detectable change in bradykinesia. A larger follow-up study where incremental changes to DBS settings are applied is needed to confirm the sensitivity of our technique. Finally, our prototype technique relies on a computer to post-process the acquired Leap Motion data. Future designs will incorporate the Leap Motion Controller with a more user-friendly interface and real-time data-processing.

Conflict of Interest

The authors have no conflict of interest to disclose in respect to this manuscript.

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