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2014

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This article was originally published at:
<https://doi.org/10.3233/JPD-140370>

Citation for this paper:

Rahimi, F., Bee, C., Duval, C., Boissy, P., Edwards, R., Jog, M., & the EMAP Group.
(2014). Using Ecological Whole Body Kinematics to Evaluate Effects of Medication
Adjustment in Parkinson Disease. *Journal of Parkinson's Disease*, 4, 617-627.
<https://doi.org/10.3233/JPD-140370>

Research Report

Using Ecological Whole Body Kinematics to Evaluate Effects of Medication Adjustment in Parkinson Disease

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Abstract.

Background: Functional motor impairments including mobility are major reasons for clinical intervention and medication adjustment in symptomatic therapy for Parkinson's disease (PD). Outcome measures used to assess the impact of medication are mostly based on patients' memory or diaries which, considering the gaps between visits, are neither objective nor very reliable.

Objective: Investigating the feasibility of using movement features extracted from ecological whole-body kinematics recordings to measure the quantitative and qualitative changes in multiple aspects of mobility after medication changes in PD.

Methods: Eleven patients with PD (PwPD) performed mobility tasks in their own home, wearing a full body wireless inertial sensing based motion capture system. Three scripted walking tasks (walking, fast walking, and walk turns) were examined at baseline and two weeks after medication changes. Clinical scales, including investigator-rated clinical global impression of improvement (CGI-I), were collected at both visits.

Results: Out of 59 recorded body joint variables, five were identified as pertinent. Changes were represented in vector space as a plot of mean versus peak amplitude. Regression analysis was used to predict clinical improvement or worsening based on these vector features. The predictors were able to explain (>98.5% of variance) patients' clinical global impression of improvement, thus correctly predicting 5 cases of improvement and 2 cases of worsening.

Conclusions: This study provided a method of extracting clinically meaningful reports from ecological kinematic data showing changes after drug adjustments. The results are presented using a novel concept called *change space* that may be more understandable for clinical staff.

Keywords: Parkinson's disease (PD), kinematics, mobility limitations, follow-up studies, biomedical engineering

INTRODUCTION

Clinicians regularly make management decisions such as pharmacological medication adjustments in

order to optimize patients' quality of life. Patients, caregivers and the medical team are all keenly interested in obtaining measures, whether subjective or objective, of the response to such medical and non-medical interventions. This information is generally gathered by clinical interviews and performances on clinical tests, and in many scenarios by objective biochemical (e.g. blood chemistry) or technological

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(e.g. cardiogram) measurements. Historical information obtained from the patient, caregivers and other sources is taken into consideration to assess the clinical state, adjust treatment and evaluate the effects of these changes at future visits. The experienced clinician combines this information along with the physical examination to make the best possible management change in order to improve the patient's quality of life.

Specifically for PD management, historical information given by patients and caregivers is usually considered as being somewhat subjective. Also rendering the evaluation of treatment difficult is the fact that evaluations done during visits to the clinic do not represent a typical state of that patient's mobility dysfunction. Accordingly, the physician performs the examination in a setting where the patient's functional state could be misjudged. Additionally, typical physical examination uses rating scales such as the Unified Parkinson Disease Rating Scale (UPDRS) which may not be ideal in the representation of global mobility dysfunction in patients with PD. Given the long gaps, commonly 6–12 months between assessments, this historical and physical assessment could provide unreliable information upon which the clinician makes management decisions.

When it comes to objective mobility assessments in PD, instrumented laboratory measurement techniques including the GaitRite mat [1, 2], optical and magnetic based motion capture systems including Optotrack [3] and Vicon [4, 5] or Polhemus Fastrak [6, 7] among others have been used in combination with performance based measures to characterize mobility features during gait and numerous functional tests [8, 9]. However, these techniques require constrained optimized environments, are expensive and rarely portable, requiring patients to come to the laboratory making them impractical for clinical use. Ambulatory mobility assessment has become a reality with recent advances in wireless technology and inertial sensing of motion for conducting field based ambulatory whole-body 3D motion capture [10–12]. These systems allow the user to record from multiple sensors and thus, provide multi-joint motion data relatively easily. Since the technology is mobile, it is possible to take the recording systems to the patient's own home environment for data collection [13, 14]. The data is transported back and analysed. However, to date, software to analyse and understand this extremely complex multi-joint data in a clinically meaningful way has not been developed. This is an important task that needs to be addressed if such tools are to be used to evaluate changes in mobility after treatment adjustments by the clinical staff.

The present study utilized a wireless wearable technology to determine the impact of drug management changes on the patient's mobility. Then, we proceeded to develop a method to facilitate the interpretation of the results in clinical meaningful way. We chose walking tasks for this pilot work as gait dysfunction is one of the most important causes of functional disability in PD.

MATERIALS AND METHODS

Subjects

The study protocol was approved by the Human Subjects Research Ethics Board (HSREB) of the University of Western Ontario. From routine visits to the clinic (London Health Sciences Centre, London, Ontario, Canada), the clinician in the research team (MJ) identified 16 patients with PD (PwPD) who required a change in their management. Eleven of them accepted to participate in the study. All eleven PwPD were tested pre- and two weeks post-adjustment in medications with changes instituted on the first day of this two week period. Enrolled PwPD met the UK Brain Bank Criteria for PD and were on stable medications for at least three months prior to enrollment in the study. The treating movement disorders specialist (MJ) determined the medication changes required to optimize patient function at a regular clinic visit (among other reasons for the medication change was to reduce dyskinesias). However, medication changes were instituted only after the first baseline kinematic assessment was completed in the patient's home. PwPD were evaluated exactly 2 weeks after the changes were commenced. No other medication changes were allowed until the follow-up clinic visit. No new assistive devices were prescribed during the study and all patients were assessed by the same physician in clinic and by the same in-home assessment team across all study visits. All investigators were blinded to all results of kinematic assessments.

Medication adjustment and changes

All individual medication changes were recorded and converted into levodopa equivalent daily doses (LEDD) using the well-accepted formula in the literature [15, 16]: $LEDD = 1.0 \times (\text{regular levodopa}) + 0.75 \times (\text{controlled release levodopa}) + 100 \times (\text{pramipexole}) + 1 \times (\text{amantadine}) + 0.33 \times (\text{regular levodopa if entacapone is administered}) + 100 \times (\text{rasagiline})$.

Self-reported outcomes

Numerous self-reported outcomes were measured by questionnaires prior to medication changes and at two weeks post medication adjustment. Outcomes included: cognitive status with the Montreal Cognitive Assessment (MoCA) [17]; Quality of life with the McGill Quality of Life (MQL) [18]; physical activity with the Phone FITT [19] and community mobility with the Life Space Questionnaire [20]. Investigator-rated 7-point Likert-style clinical global impression of improvement (CGI-I) [21] was also collected at the patient's subsequent clinic visit while the clinician was not made aware of any of the study data/results. These served as benchmark to determine whether the changes detected with the sensor system were related to clinical changes detected by the aforementioned evaluations.

In-home kinematic assessment

Recording Equipment: The kinematic equipment used was the Functional Assessment of Biomechanics (FAB) system made by BioSyn® Systems Inc. The FAB System is a wireless motion capture system that uses a network of inertial measurement units (IMUs) positioned on specific body segments of an individual to determine their orientation and compute relative angular displacement of each limb according to a biomechanical model. Thirteen lightweight sensors ($4 \times 7 \times 2.4$ cm) were attached by a research assistant to standardized locations on the participant's body segments including head, upper and lower arm, thoracic trunk, pelvis, thigh/shank and leg. Elastic straps were used to guarantee stable fixation. An auto-calibration routine was performed according to the manufacturer's procedures before each data collection session. The data were sampled and collected at 100 Hz and transmitted wirelessly to a small receiver system connected to a laptop.

Tasks Evaluated: Scripted tasks were evaluated in the in-home assessment. They were: walking (W), walking turns of 180° (WTL) and fast walking (FW). All patients performed these tasks pre- and two weeks post-medication adjustment. Each task was performed three times. Testing was administered at approximately the same time of the day, on the same day of the week for pre- and post-tests, and between patients.

Data Analysis: All of the following analyses were conducted separately for pre- and post-medication adjustments. All recorded trials were screened for possible abnormal/unreliable data sections before

being processed. Epochs of each task were manually extracted for analysis by watching the avatar animation time-synchronized with the recorded data. The proprietary FAB algorithm fused the data in each IMU, determining the sensor's orientation and acceleration in space, and then provided joint angle and angular velocity for each joint over time for a total of 59 joint variables. A first layer of analysis consisted of identifying joint variables that are most relevant to the tasks at hand. The method for the data reduction (to 5 contributing variables) is described in detail in Appendix A.

In order to describe the characteristics of the movement recorded from each of the joints, we assessed two important features. These two features were based upon the hypothesis that for every joint, the movement needs to have not only a reasonable amplitude, but also needs to be smooth in its implementation. The combination of amplitude and its smoothness would aid in performing a task effectively. For instance, a moderate increase in mean value and a stable peak value would be desirable, especially if the pre-test indicated the presence of bradykinesia. Conversely, a marked increase in peak and mean values could be consistent with dyskinesia. Therefore, to quantify the effect of intervention on each of these 5 contributing variables while performing the task, mean and peak amplitude values of each variable were calculated over the entire trial.

These (mean and peak) values were then compared before and after the medical intervention (Supplementary Figure 1B shows such results for a trial of walking). Since the scales of movement for each variable were different (e.g. joint angles for different joints, or angles versus angular velocities), z-scores were calculated separately for each of the contributing variables for all subjects and all trials, and for pre and post intervention. To present the effect of intervention on the kinematics of task performance, changes in z-score of the 5 contributing variables are plotted as vectors. Supplementary Figure 1C shows an example of such a presentation for the walking task of patient 1.

In order to determine consistency in the kinematic changes for each participant, the change vector plots analysis was repeated for that participant for the three tasks evaluated (W, FW and WTL) as our standard presentation method. Each change vector represented the average of the 3 trials for each task. In this way, the 3 tasks yielded a total of 15 such change vectors for every participant. The change vectors could point in any orientation from 0° to 360° in the z peak /z mean plane, and are also characterized by their ampli-

tude. Vectors are represented with z-score change in the x-axis, and by peak value z-score in the y-axis (Supplementary Figure 1C). This vector space was further divided into eight 45 degree portions, Q1 to Q8 in an anticlockwise direction (see Supplementary Figure 1D). This space was termed *change space*. Such a division allowed for comparison between the mean and peak values for the change vectors. Given that any relative mean and peak change is possible, similar changes (Q2, Q4, Q6, Q8) and relative changes with either mean or peak dominance (Q1, Q3, Q5, Q7) are easily categorized. For example, Q1 represented a main increase in peak, Q2, a comparable increase in mean and peak, Q3 an increase mainly in mean etc. So, for each joint variable, change space helps to classify the type of change and hence clinical interpretation.

Change vectors in z-space allowed both quantitative and qualitative evaluation of change in mobility after medication intervention. Also, as each vector has by definition a direction and amplitude, the 15 change vectors presented the overall change direction (the count of vectors in each of the 8 portions, NQ1-NQ8) and overall change magnitude (the average magnitude of vectors in each of these 8 portions, L1-L8). By this classification and analysis, magnitude and direction of vectors are used to illustrate changes in task performance, representing mobility change, and quantifying its improvement or worsening.

Subsequently, in order to confirm clinical meaning of such overall direction and magnitude of change, a regression analysis was conducted to predict non-kinematic (scale based) outcome measures. In order to deal with the sparsity and high dimensionality problem (we had 11 patients but 16 variables (NQ1-NQ8 and L1 to L8)), the LASSO (Least Absolute Shrinkage

and Selection Operator) technique [22] was applied, which reduced the number of predictors as explained and summarized in Appendix B.

RESULTS

Patient demographics

The demographics of the patients are summarized in Table 1. Eleven patients (8 males, age 67.5 ± 7.4 , diagnosed using conventional criteria, with a Hoehn and Yahr score 2-3, 1 drug-naïve, 1 required walking aid, 8 led fairly active lifestyles) were recruited from the movement disorders clinic, and participated in the study. The disease duration varied from 2 to 17 years with the average duration being 8.1 years.

Clinical rating scales

Antiparkinsonian medication dosages (including regular levodopa, controlled release levodopa, pramipexole, amantadine, entacapone, rasagiline, and ethopropazine) had an average LEDD of 845 mg at baseline, and an average increase of 24%. The patients showed an average increase of 4.2, 1.6, and 0.6 in Phone-FITT (/100), MoCA (/30), and MQOL (/10) scales respectively. The increase in MoCA scores was significantly higher than zero (z-test, $p < 0.05$). However, none of the other scales were significantly different from baseline (two-tailed, paired *t*-test).

Kinematic Data: The change in z-score for the contributing variables' peak and mean values during the walking task is presented in Fig. 1 for each of the eleven patients. The x-axis represents the peak while the y axis the mean amplitude of the change in that variable. The kinematic analysis clearly shows that, as expected, the

Table 1
Demographics, CGI-I, medication levodopa equivalents, and self-reported and clinical scales pre and post medication adjustment

Patient ID	AGE/Gender	Disease Stage (H&Y)	Disease Duration	CGI-I	LEDD Pre/Post	Phone-FITT Pre/Post	Life-Space Pre/Post	MoCA Pre/Post	MQOL Pre/Post
1	78-M	2	8	3	400/600	9/11.2	6/6	28/29	6/8
2	57-F	2	14	2	1248/11348	55/62.5	5/7	26/29	7/8
3	56-M	2.5	9	-2	600/600	59/42	6/5	30/29	6/7
4	64-M	2	3	2	0/400	71.5/72	7/6	23/29	7/8
5	73-M	3	2	-2	1300/1100	6/6	6/6	23/23	10/8
6	62-F	2	5	0	1350/1950	30/55	5/5	21/26	5/9
7	75-M	3	6	0	1064/1596	9/18	4/5	26/27	6/5
8	74-F	3	17	0	1050/1250	42.5/64	5/5	18/23	10/9
9	65-M	2	3	0	600/800	27/14	5/5	23/22	6/5
10	71-M	3	12	1	750/950	17.5/32.2	6/6	20/22	8/10
11	67-M	2.5	10	1	900/900	42.5/38.8	7/5	21/17	7/8
AVG±SD	67.5 ± 7.4	2.5 ± 0.5	8.1 ± 4.9	0.5 ± 1.6	845 ± 424 1048 ± 472	33 ± 22 38 ± 23	6 ± 1 6 ± 1	24 ± 4 25 ± 4	7 ± 1.6 8 ± 1.6

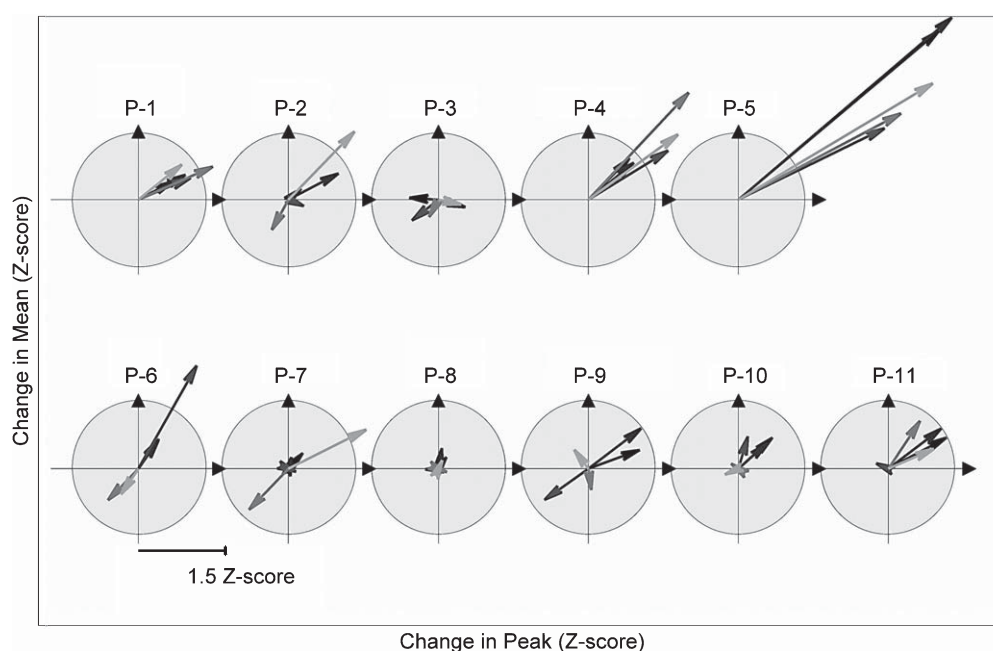


Fig. 1. Walking compared for all patients. The plots are shown on the same scale to allow a direct visual comparison among all of the patients. Vectors point in different directions (Q1 through Q8) with the amplitude of the vector defining the quantity of change. The change in z-score for the 5 contributing variables' peak and mean values during the walking task for each of the 11 patients is presented as an example. Each vector's size and direction denotes both the qualitative and quantitative change in that variable. Overall change in walking for patients P-1, P-4, P-5, P-10, and P-11, having vectors dominantly in Q2, is expected to be clinical improvement whereas for P-3 it is not. In addition, P-5 is expected to have excessive movements or dyskinesia. Length of 1.5 z-score is marked under the plots for visual comparison.

range, direction, and the relative amount of change in peak and mean values are substantially different among the participants. The change in each individual patient and the profile of these changes is shown in Fig. 1 as an example for the walking task. In 5 out of the 11 cases, the vectors predominantly ($\geq 50\%$) point towards Q2, in 1 case the vectors were predominantly in Q6 while in the remaining 5 cases, the vectors pointed towards two directions. However in four of these remaining 5 cases, the vectors were distributed between Q2 and another direction (Q1, Q5, and Q6). This implies that overall, 9 out of 11 cases had the change vectors predominantly pointing towards Q2. Depending on the starting point of each variable within the change space this directional change pointing towards Q2 could be considered to reflect a favorable change in the mobility. In these patients, comparison to the CGI-I confirms that the clinical intervention was generally either very effective or moderately effective for those patients.

The results of regression analysis comparing kinematic and non-kinematic scale based measures indicated that 7 out of 11 predictors (NQ1,2,4,8, L1, 2 and 6) explained 98.5% of the variance in the CGI-

I ($R^2 = 0.985$, $F(7,11) = 36.39$, $p < 0.01$). Additionally, these seven predictors significantly predicted the CGI-I score which implies that the number and the length of vectors in some of the Q1-8 portions have meaningful relation to patients' overall improvement/worsening (Appendix B).

As presented in the Appendix B, reduced aspects of 15 vectors were also able to significantly predict the other clinical (patient) scales. For example, nine of these predictors were able to explain 100% of variance in Phone FITT questionnaire's change.

Figures 2 and 3 are representative examples of positive and negative outcomes of interventions. In Fig. 2, the increase in levodopa produced a measureable positive change in the kinematics where the vectors show an increase in mean amplitude and often a comparable increase in peak (dominantly in Q2). For the patient shown in Fig. 3, levodopa and rasagiline were added to the medication regime. However, there was an overall worsening of the patient's kinematics with the mean and peak amplitude for all three tasks dropping overall (NQ6 = 8).

In these two examples, kinematic estimation of improvement or worsening is also reflected in the clin-

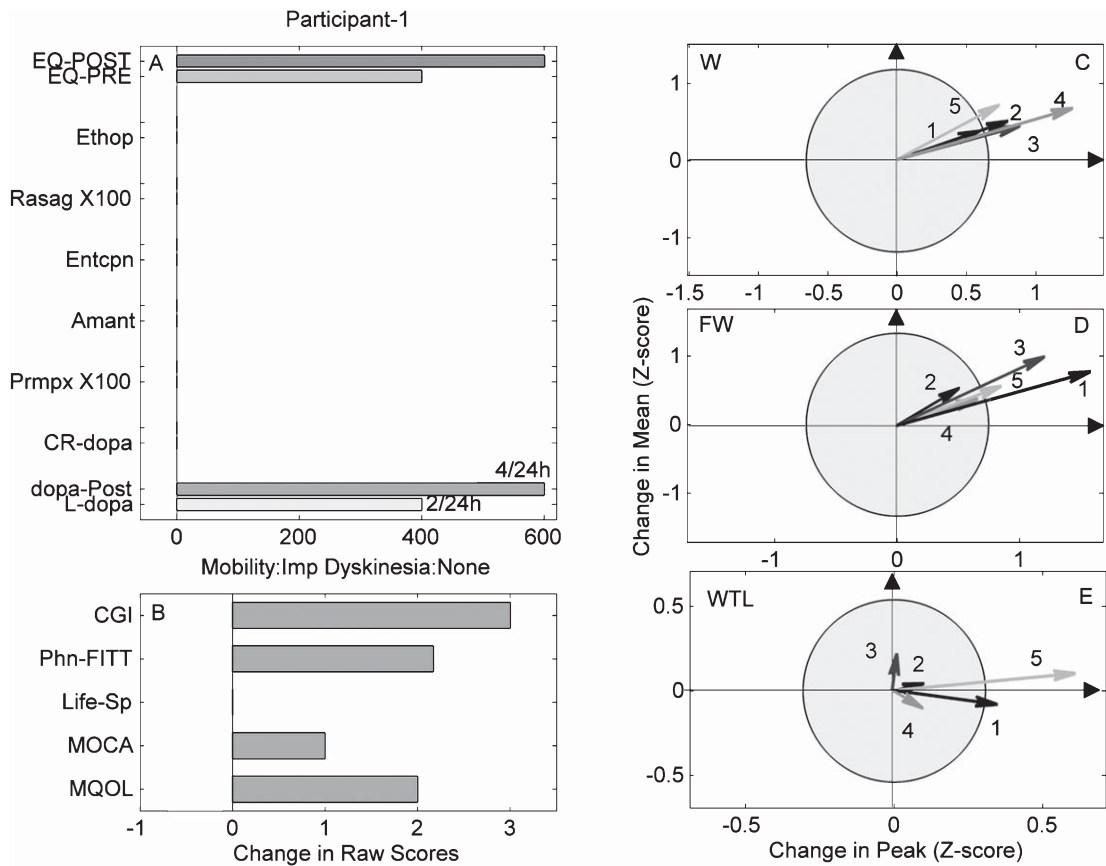


Fig. 2. A sample patient with improved mobility. A case where the medication adjustment produced a significant improvement is shown. Summary of medication dosage and timing pre and post adjustment are presented in (A). The only antiparkinsonian medication, regular levodopa was increased from 400 mg to 600 mg. Change in clinical scores, including CGI-I, within the 2-weeks is shown in (B). Four of the five clinical measures of function show an improvement in raw scores. The kinematic analysis shows that 11 of the 15 vectors plotted in walking (C), Fast Walking (D) and turning left while walking (E) show a dominant direction of change in Q2. This implies an improvement in mean and peak values (predictor values for CGI-I, [NQ1, 2, 4, 8, L1, 2, 6] were [2, 11, 0, 1, 0.49, 1.01, 0] respectively). EQ-POST and EQ-PRE are Levodopa equivalents pre and post. Ethop = Ethopropazine, Rasag = Rasagiline, Entcpn = Entacapone, Amant = Amantadine, Prmpx = Pramipexole. Patient reports show mobility improvement and no observed excessive movement (dyskinesia).

ical measures shown in Figs. 2B and 3B along with the medication details in Figs. 2A and 3A.

DISCUSSION

Evaluating how a change in the medication regimen may affect patients' mobility, especially in their natural environment, remains a difficult challenge. Here, we demonstrated that it is possible to detect changes in individual patients' overall mobility following medication adjustment, whether there was improvement or worsening in gait, and presence or absence of dyskinesia. We also demonstrated that it is possible to reduce the data to a few meaningful variables provided by a reduced number of body joint variables

(sensors). Finally we have demonstrated the feasibility of representing complex biomechanical data in a more clinically meaningful way. In the present study, mobility changes were kinematically measured and correlated with clinical (physician- and patient-based) parameters of change pre- and post-intervention. Each patient had a unique effect in response to the intervention being made, as expected, and this was captured as either a positive (improvement) or negative (worsening) change. Fifty-nine variables were generated from the recordings of overall whole body mobility, in the form of joint angle, velocity, etc. across 3 common everyday tasks. The degree to which each variable contributed to representing each particular task was different, but remained consistent within each of the 3 tasks. As expected, those variables that reflected hip,

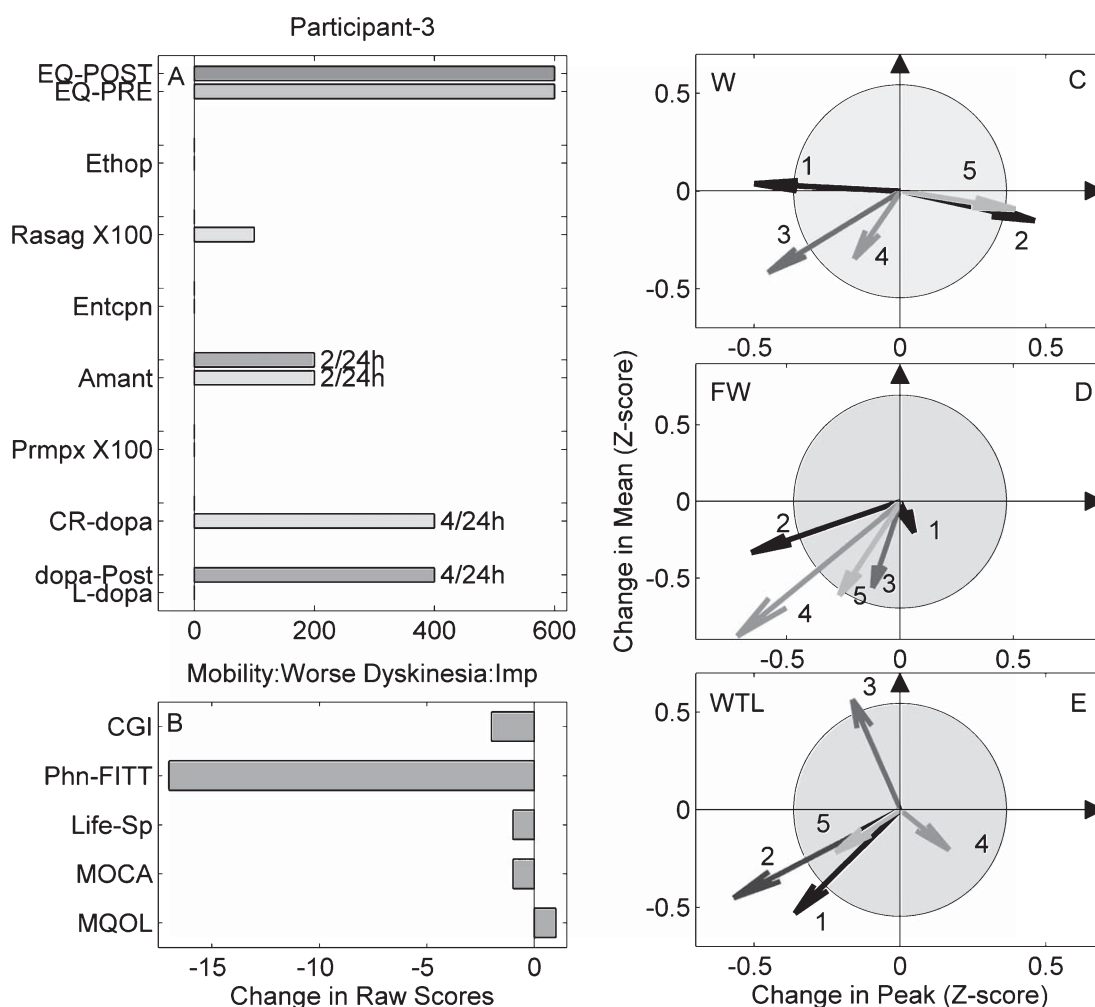


Fig. 3. A sample patient with worsening in mobility. A case where the medication adjustment produced a worsening effect is shown. Summary of medication dosage and timing pre- and post-adjustment is shown in (A). In this example, the patient had an addition of 400 mg of Levodopa and 1 mg of Rasagiline to an already existing dose of controlled release levodopa. Changes in clinical scores, including CGI-I, within the 2-weeks (B) are mainly towards the negative implying worsening. The kinematic analysis shows that 11 of the 15 vectors plotted in walking (C), Fast Walking (D) and turning left while walking (E) show a direction of change in Q6 to Q8. This implies a dominant worsening in mean values (predictor values for CGI-I, [NQ1, 2, 4, 8, L1, 2, 6] were [2, 0, 0, 1, 0.45, 0, 0.65] respectively). EQ-POST and EQ-PRE are Levodopa equivalents pre and post, Ethop = Ethopropazine, Rasag = Rasagiline, Entcpn = Entacapone, Amant = Amantadine, Prmpx = Pramipexole. Patient reports a worsening in mobility and improvement in dyskinesia.

knee and upper limb measurements were the most relevant to overall walking with 5 variables which stand out as being the most contributory in representing each of the tasks.

In order to illustrate these kinematic change quantities, we developed the concept of *change space*. Within this *change space*, the change in amplitude of the mean values in each of the five variables is believed to represent a change in the amount of movement that has occurred. The change in amplitude of the peak values can be thought of as representing a change in the level of smoothness of the signal. Clinically, one can

imagine a scenario where the mean and peak amplitude increased, but the size of the vectors is not too large. This change could be interpreted as favorable where the quantity of movement increased and the degrees of liberty also improved. In contrast, a large peak amplitude change with small mean amplitude change may be interpreted as a jerky signal, consistent with dyskinesia [23–25]. Such an approach allows the *change space* to be interpreted in a clinical context. It is important to note that the interpretation (improvement or worsening of the patient mobility) of the direction of the change vectors is dependent on the pre-intervention kinematic

state of the patient. Therefore, if baseline or kinematic pre values (both mean and peak) are of moderate amplitude, vectors pointing towards Q4, 5 or 6 may represent an improvement in overall mobility suggesting that the peak amplitude for that variable have been reduced. Clinically, this scenario can represent a reduction of dyskinesic movements. Similarly, if a patient is bradykinetic without dyskinesia one favorable kinematic outcome could be change vector direction in Q2. In this fashion, the *change space* can be quantitatively used to make a clinical interpretation of where the patient's mobility was before medication change, and where it ended after intervention. Clinical experience and patient outcomes can thus be objectively translated into clearly objectified measures.

Despite the differing patient profiles and management changes that were made, the results shown in the two examples above indicate that the method we have developed may be used to show clear categories of functional change. Our novel construct of *change space*, using peak and mean changes in kinematic variables that represent mobility is thus clinically relevant and could help the clinician make interventions based on potentially more reliable, consistent and objective data than clinical or patient-based scales alone. Kinematic analysis could be considered a valid tool for assessment of patient clinical states pre- and post-intervention.

LIMITATIONS OF THE STUDY

Contrary to other studies which focus on assessing symptomatology, the present study focused on how effective the change of medication on daily activities may be, which is more important for patients. With no baseline being presented in our *change space*, the clinician needs to interpret the overall direction and magnitude of change vectors (to be improvement or worsening) knowing the clinical state of the patient before the medication change. Only then, the clinician will be able to appreciate the amplitude and direction of the change space vectors. For instance, if medication change reduces the targeted symptom (e.g., dyskinesia), but induces bradykinesia, medication change could be considered as ineffective if the motor repertoire is reduced [26].

CONCLUSIONS

In this pilot study, we have demonstrated the feasibility of using inertial sensor technology to assess

PwPD within the home environment. Our novel concept of *change space* provides a new approach towards objectively capturing not only quantity, but also quality of movement, and transforming biomechanical data into clinically relevant information that can be used by clinicians to assess the impact of their treatment modifications on patients. Such objective assessment of mobility can be a more accurate and relevant outcome measure in clinical trials. Analyzing and sharing the movement patterns with patients in their follow up visits can raise self-awareness and possibly motivate them to adapt their lifestyle, and hence improve their quality of life.

ACKNOWLEDGMENTS

Authors acknowledge substantial contributions of Monica Jog to acquisition of data. This study was partially funded by Canadian Institutes of Health Research (CIHR), and Parkinson Society Canada.

FINANCIAL COMPETING INTERESTS

None of the authors had financial interest to report.

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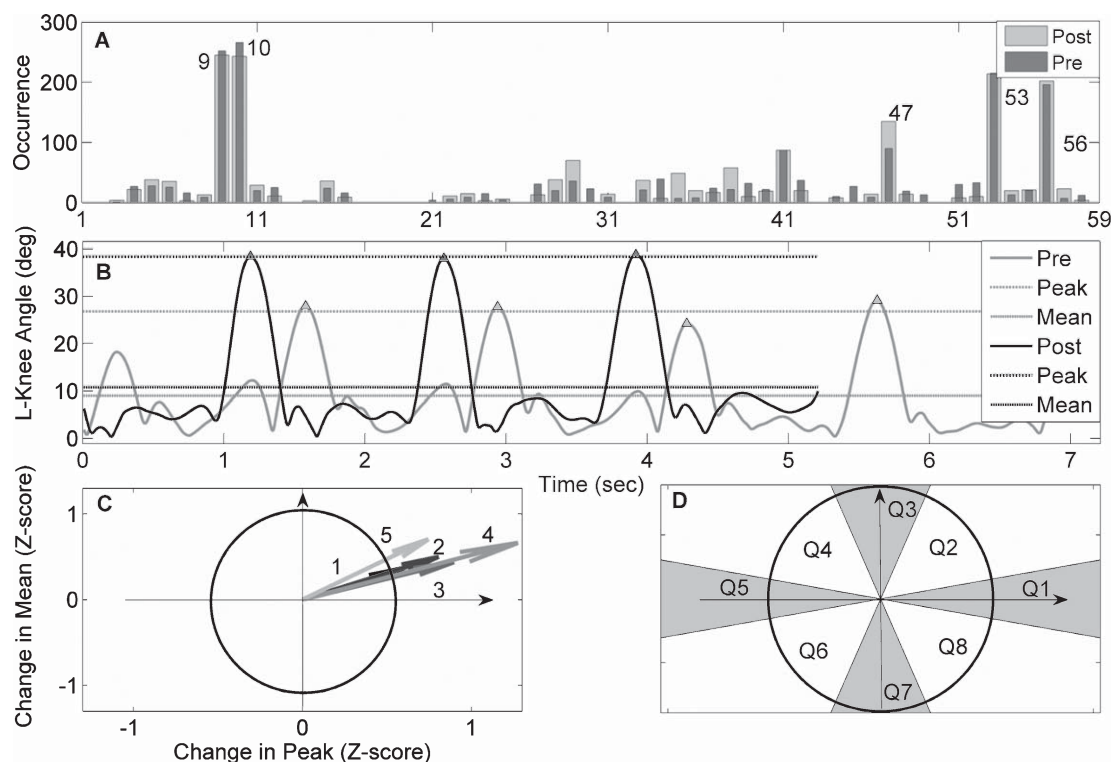
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APPENDIX A

Reduction of 59 Body joint variables during each task

A total of 59 joint variables were collected during task performance, but involvement of these variables may not be equal during performance of that task. Therefore, in order to find the most contributing variables to performance of each task, involvement of these 59 variables were ranked, and the top 5 were kept for further analysis. For each trial, all 59-variables were averaged in bins of 0.1 and 0.2 s. Since there was no effect of bin size on the outcome (selecting the most contributing variables), the data for the bin size 0.2 s was used and normalized to either largest angle or largest velocity across all subjects. The reason for doing this is to be able to treat both groups of variables (angle or angular velocity) equally. For evaluation of each trial of a task for every participant, 59 variables were reduced to 10 variables with highest variability (variance). The occurrence and rank of these 10 variables were considered for the 3 trials performed by each of the 11 patients. The weighted sum (weight of 10 for first rank, 9 for the second rank, etc.) of the occurrence of these ten variables is presented for the walking task (Supplementary Figure 1A). The top five variables with consistent and highest rank order across all trials were selected as being the most contributing variables allowing reasonable data reduction for further analysis. These five variables will be called *contributing variables* for brevity.

To quantify the effect of intervention on each of these 5 contributing variables while performing the task, non-binned, non-normalized data were used to calculate both mean and peak amplitude value of each variable over the entire trial. Supplementary Figure 1B shows such results for a trial of walking. Since the scales of movement for each variable were different (e.g. joint angles for different joints, or angles versus angular velocities), z-scores were calculated separately for each of the contributing variables. To present the effect of intervention on the kinematics of task performance, changes in z-score of the 5 contributing variables are plotted as vectors. Supplementary Figure 1C shows an example of such a presentation for



Supplementary Figure 1. Data reduction and change space vectors. A) Weighted sum of occurrence of ten contributing joint variables in performing each of the 3-trials of the walking task by the 11 patients. The 5 most contributing variables are: 9, 10, left-right knee angular velocity; 53, 56, left-right knee flexion angle; 47, right-hip flexion angle; B) Peak and mean values for left knee flexion angle, the third top-variable pre- and post-intervention for patient-1 in walking trial-1; C) Change in z-score for all 5 variables post-intervention, average of 3-trials of walking for patient-1 shown as vectors. The x-axis is peak while the y-axis is mean amplitude for each variable. D) Schematic of eight 45° portions of change space with the X-axis showing change in peak and y-axis change in mean z scores.

the walking task of patient 1. To address orientation of vectors, the 360 degree range of vector orientation was further divided into eight 45 degree portions, Q1 to Q8 in an anticlockwise direction (Supplementary Figure 1D). This space was termed change space.

APPENDIX B

Regression Analysis: Kinematics predict clinical scales

Regression analysis was employed to predict CGI-I and change in PhoneFITT scales based on 16 factors representing change in kinematic variables. The reduced variables were considered as the possible predictors in the linear regression analysis. Multiple stepwise regression (with backward elimination) analysis was used to test if these aspects of the 15 vectors, representing the kinematic parameters' change during

Supplementary Table 1
Predictors of the two clinical scales

	CGI-I	Δ -PhoneFITT
Q1	-0.7	
Q2	0.8	-0.4
Q3		6.3
Q4	0.6	9.4
Q5		1.5
Q6		
Q7		-21.8
Q8	-1.8	6.1
L1	0.8	-13.2
L2	-2.4	1.1
L3		
L4		
L5		
L6	2.1	28.5
L7		
L8		
Multiple R	1.0	1.0
Significance	0.0	0.0
R-squared	1.0	1.0
Adjusted-R	0.7	0.5

the three tasks, significantly predicted the mentioned two clinical scales. The final numbers of predictors and the goodness of fit, which were different for each scale, are shown in the Supplementary Table 1.

For example, the values in the table for CGI-I mean that these seven predictors significantly predicted the CGI-I score (all significant, $p < 0.05$; $\beta = -0.74, 0.75,$

$0.59, -1.84, 0.85, -2.44, 2.06,$ for NQ1, 2, 4, 8 and L1, 2, 6 respectively). This implies that CGI-I is positively correlated with the vectors being in Q2, Q4 and negatively correlated to the vectors being in Q1, Q8. Average length of the vectors in Q1 (L1) and Q6 (L6) were positively correlated while in Q2 (L2) the vector length was negatively correlated to the CGI-I.