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Short communication

Reproducibility and responsiveness of gait initiation in Parkinson's disease

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ABSTRACT

Persons with Parkinson's disease (PD) have significant impairments in functional mobility, including the ability to initiate gait. Three-dimensional analysis of kinetic and kinematic outcomes has become one of the most powerful tools in evaluating abnormalities in gait initiation for persons with PD. Surprisingly however, the psychometric properties of spatial and temporal measures of gait initiation for persons with PD have not been established using force-platforms. The purposes of this study were to determine the reliability of kinetic and kinematic measures of gait initiation and to identify the minimal detectable change of these measures in persons with PD during On and Off medication conditions. Sixteen participants with idiopathic PD performed a series of 3 repeated trials of gait initiation by starting from a quiet stance position on 2 AMTI OR-6 force platforms, and walking forward across the floor following a signal from the investigators. Testing was performed first in the Off medication condition, after which participants took their medication and waited 60 min before repeating the gait initiation assessments. Relative test-retest reliability was good-to-excellent for most outcome measures (range 0.417–0.960). Bland-Altman analysis revealed no systematic variance in the majority of outcome measures when tested in distinct medication conditions (On vs. Off medication). Most outcome measures required low-to-moderate amounts of change (<50%) to indicate true change in individual participants. These results suggest that spatial and temporal measures of gait initiation using force-platforms are highly reliable and responsive to changes in performance for persons with PD, regardless of whether individuals are optimally medicated.

1. Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder affecting approximately 4.5 million people in the world's 10 most populous countries (Dorsey et al., 2007). Performance of gait represents one of the foremost determinants for quality of life and independence for persons with PD. However, Parkinsonian gait is characterized by reductions in the size and speed of functional movements, including during the initiation of gait (Dibble et al., 2004a, 2004b).

Gait initiation (GI) research in persons with PD has traditionally been used to discriminate varying levels of disease severity (Dibble et al., 2004a; Schlenstedt et al., 2017), or to evaluate changes in motor function longitudinally (Galna et al., 2015). However, in order for kinetic and kinematic data to be useful as an evaluative or discriminative outcome measure, it must be established on sound psychometric properties. Surprisingly, the psychometric properties of these measures of GI in persons with PD have not been established using three-dimensional systems. Reliability data has been provided for persons with PD wearing inertial sensors (Mancini et al., 2016), but there is no information regarding the reproducibility or the responsiveness of three dimensional spatiotemporal outcomes of GI from force platforms.

The objectives of this study were to identify the reproducibility of spatiotemporal properties of GI events using three-dimensional kinetic and kinematic analysis, and to define the responsiveness of these measures in persons with PD during On and Off medication conditions.

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2. Methods

2.1. Participants

Sixteen people with idiopathic PD participated in this study (sample size estimations can be found in Appendix A). Participants were all enrolled in a randomized controlled trial investigating the physiologic adaptations to eccentric resistance training in persons with PD (Dibble et al., 2009) and all outcomes reported in this study were gathered at baseline, prior to any intervention. All participants provided informed consent as approved by the University of Utah Institutional Review Board.

Participants (Table 1) were included if they had a physician confirmed diagnosis of mild to moderate idiopathic PD (Hoehn and Yahr 1–3), were between 40 and 85 years of age, and were willing and able to comply with a 12-week resistance training program. Exclusion criteria can be noted as previously described (Dibble et al., 2009).

2.2. Measurement of GI

Participants arrived at the assessment facility in the morning having not taken their prescribed medication for at least 12 h. Testing was performed first in the Off medication condition, after which participants took their medication and waited 60 min before performing the assessments again. GI trials were captured using 2 AMTI OR6 series force platform systems (AMTI; Watertown, USA). One foot was placed on each platform, which were located at the start of a 1- by 5-meter walkway demarcated by solid color butcher paper. Each individual's feet were traced with a marking pen and these tracings were used as the starting position for all GI trials. A 8-camera VICON™ motion system (Vicon Motion Systems Ltd, Oxford, England) was used to sample the 3-dimensional motion of reflective markers placed on the participant based on a standardized gait analysis marker set defining 15 body segments (Plug-In-Gait marker set; Vicon Motion Systems; Oxford, UK). Sampling and filtering parameters can be found in Appendix B.

In order to examine self-initiated gait patterns, each individual was asked to gaze forward and stand as quiet and still as possible in a natural initial posture. While wearing comfortable shoes, participants were instructed to "begin the walking process as quickly as possible and continue walking to the end of the walkway." The self-initiated tasks were performed 3 times in the On and Off medication conditions (Bonora et al., 2017; Mancini et al., 2016).

2.3. Three-dimensional analysis of GI

Temporal and spatial measures of GI were extracted with the VICON™ motion capture system. Temporal data was measured as the duration of time spent in each GI phase, modified based on previous research (Hass et al., 2005). (1) The Imbalance phase was defined as time (s) between onset of Center of Pressure (CoP) displacement and heel-off of the swing limb; (2) The Unloading phase was characterized as the time (s) between heel-off of the swing limb and toe-off of the swing limb; (3) The Propulsion phase was defined as the time (s) between toe-off of the swing limb and heel-strike of the swing limb. The CoP trajectory during each of these phases can be seen in Fig. 1.

Spatial outcome measures included: Step length (m), CoP displacements (m) in posterior and lateral directions, and Center of Pressure – Center of Mass (CoP-CoM) displacements (mm) during the Imbalance and Propulsion phases of GI (Dibble et al., 2004a; Halliday et al., 1998; Martin et al., 2002). See Appendix C for a description of variables.

Table 1
Participant demographics.

Characteristic	Value
Age	68.0 ± 12.0
Sex	10 M/6F
Years with disease	7.76 ± 4.5
Affected side	9 R/7 L
Hoehn & Yahr (H&Y)	2.5 ± 0.5
UPDRS On medication	12.53 ± 7.3
UPDRS Off medication	24.71 ± 8.6

R-Right; L-Left; UPDRS – Unified Parkinson Disease Rating Scale (motor section). Values are mean ± standard deviation; H&Y is median ± standard deviation.

2.4. Data analysis

Relative and absolute reliability, and minimal detectable change (MDC) scores were factored from the mean of 3 individual GI trials. Bland-Altman plots and regression analyses were used to assess mean differences in spatiotemporal measures between sessions (On vs. Off medication). SPSS (version 25.0) and Microsoft Excel (version 16.0) were used for all statistical analyses.

2.4.1. Relative reliability

We calculated relative reliability using the ICC (3,3) via SPSS in a two-way mixed model with absolute agreement.

2.4.2. Absolute reliability

We assessed measurement error for within-subject variability across repetitive trials using the SEM and %SEM. The SEM is indicative of the range of scores that can be expected on retesting (Portney and Watkins, 2009). The %SEM is used to express measurement error in a fashion that is independent of the units of measurement. %SEM provides an indication of the smallest change that is representative of true change for a group of individuals (Flansbjer et al., 2005). Calculations for SEM and %SEM can be found in Appendix D.

We further assessed absolute reliability of spatiotemporal measures by assessing their consistency across distinct medication conditions (On/Off medication). Bland-Altman plots were

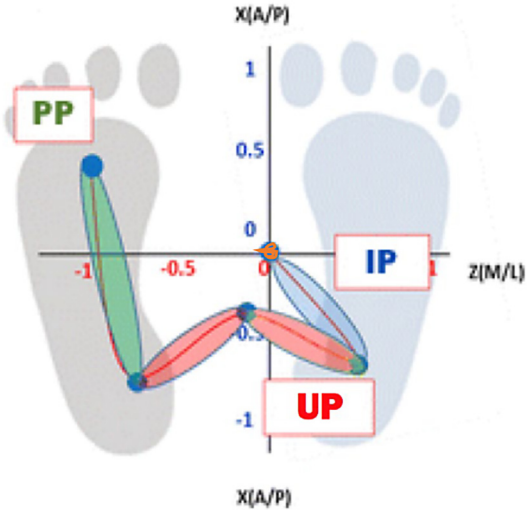

Fig. 1. Center of Pressure (CoP) trajectory of a sample participant during the Imbalance (IP), Unloading (UP), and Propulsion (PP) phases. The orange colored trajectory at 0,0 represents the 0.85 s window of quiet standing prior to gait initiation. Image adapted from Cimolin V et al., *J Neuroeng Rehabil* 2017, 14(1), 44. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

constructed by plotting the between-session difference for each variable when participants were On medication versus Off medication, against the mean for each variable (Bland and Altman, 1986). Systematic trends and outliers were identified using the 95% confidence intervals (CI). Linear regression was then used to identify the presence or absence of nonuniform relationships (proportional bias) in spatiotemporal variables assessed during distinct medication conditions.

2.4.3. Responsiveness

The MDC, which represents the minimal amount of change that is not due to variation in measurement at a specified CI (Haley and Fragala-Pinkham, 2006), was calculated for the 95% CI. The MDC was also expressed as a percentage in order to be interpreted independently of the units of measurement using %MDC. The %MDC is indicative of the smallest change that represents true change in a single person (Flansbjer et al., 2005). Calculations for the MDC and %MDC can be seen in Appendix E.

3. Results

3.1. Relative reliability

ICCs that range from 0.40 to 0.59 are considered fair, those that range 0.60–0.74 are good, and >0.75 are considered excellent (Cicchetti, 1994). Based on these criteria, relative reliability from test-retest assessments was good-to-excellent (0.66–0.960) for most of the spatiotemporal measures of GI during On-medication assessments. The Off-medication trials all yielded excellent relative reliability (0.783–0.945).

3.2. Absolute reliability

Measurement error (%SEM) was low for all measures of GI (<30%) regardless of medication condition (Table 2). Similar % SEM values were found for nearly all outcome measures between medication conditions. Measurement errors increased systematically for nearly all variables in the Off-medication state relative to On-medication.

We assessed absolute reliability of spatiotemporal measures that were taken during contrasting medication conditions only using variables that had good-to-excellent relative reliability within-subjects (ICC > 0.60; Table 2). To do so, we used Bland-Altman statistics to examine systematic variances in On versus Off medication periods. Bland-Altman plots revealed no systematic variance between sessions (i.e., zero was included in 95% CI) for most of the variables. Systematic variance was noted (i.e., zero was not included in 95% CI) only for the mean differences in CoP-CoM displacement (mm) during the Propulsion Phase (Fig. 2B).

We further investigated the stability of mean differences for each variable in On versus Off medication periods by use of linear regression. Regression analyses revealed no uniform variability for the majority of spatiotemporal measures. Only the mean differences for On vs. Off medication assessed using the duration of time in the Imbalance Phase ($F(1,15) = 9.28$, $P = 0.009$) (Fig. 2C) and the magnitude of the Lateral CoP shift ($F(1,15) = 19.04$, $P = 0.001$) demonstrated nonuniform relationships (proportional bias). A discussion on this finding can be found in Appendix F.

3.3. Responsiveness

Lower %MDC values are indicative of greater responsiveness than higher %MDC values. The %MDC values ranged from 11.5% to 92.8%, with the lowest values being found for the Propulsion Phase and the highest values found during the Posterior CoP shift. The introduction of dopamine replacement medication had little effect on responsiveness. In nearly all cases, responsiveness was slightly greater (lower %MDC) during On-medication states than when participants were assessed Off medication (Table 2).

Table 2
Means and Standard Deviations (SD), 95% Confidence Intervals (95% CI), Intraclass Correlation Coefficient (ICC), Standard Error of Measurement (SEM), % Standard Error of Measurement (%SEM), Minimal Detectable Change utilizing a 95% confidence interval (MDC_{95}), and % Minimal Detectable Change (%MDC) for temporal and spatial measures of gait initiation in people with Parkinson's disease on and off medication.

Outcome Measure	Mean (SD)	95% CI	ICC	SEM	%SEM	MDC_{95}	%MDC
Imbalance phase (s)							
On	0.44 (0.09)	0.39–0.48	0.828	0.04	8.62	0.13	29.3
Off	0.51 (0.19)	0.41–0.61	0.842	0.07	14.43	0.25	49.0
Unloading phase (s)							
On	0.14 (0.03)	0.13–0.16	0.571	0.02	13.07	0.06	44.4
Off	0.18 (0.06)	0.15–0.21	0.810	0.03	14.54	0.09	49.4
Propulsion phase (s)							
On	0.36 (0.05)	0.33–0.39	0.908	0.02	4.37	0.05	14.8
Off	0.37 (0.05)	0.34–0.39	0.860	0.02	5.43	0.07	18.4
Step length (m)							
On	0.43 (0.12)	0.36–0.49	0.960	0.02	5.68	0.08	19.3
Off	0.38 (0.09)	0.33–0.43	0.922	0.03	6.93	0.09	23.5
Posterior CoP shift (mm)*							
On	28.71 (11.58)	22.2–35.2	0.702	6.32	22.02	21.46	74.7
Off	24.68 (14.49)	17.2–32.1	0.783	6.75	27.35	22.91	92.8
Lateral CoP shift (mm)*							
On	41.13 (13.25)	34.5–47.7	0.766	6.41	15.58	21.76	52.9
Off	38.37 (20.33)	28.2–48.5	0.912	6.03	15.72	20.47	53.4
Imbalance phase CoP-CoM distance (mm)*							
On	101.08 (12.56)	94.8–107.3	0.417	9.59	9.49	32.56	32.2
Off	100.12 (28.57)	85.8–114.4	0.945	6.70	6.69	22.75	22.7
Propulsion phase CoP-CoM distance (mm)*							
On	207.35 (37.35)	188.1–226.5	0.667	21.55	10.39	73.17	35.3
Off	184.62 (36.11)	166.4–202.7	0.932	9.42	5.10	31.91	17.3

*CoP: center of pressure.
*CoP-CoM: center of pressure – center of mass distance.

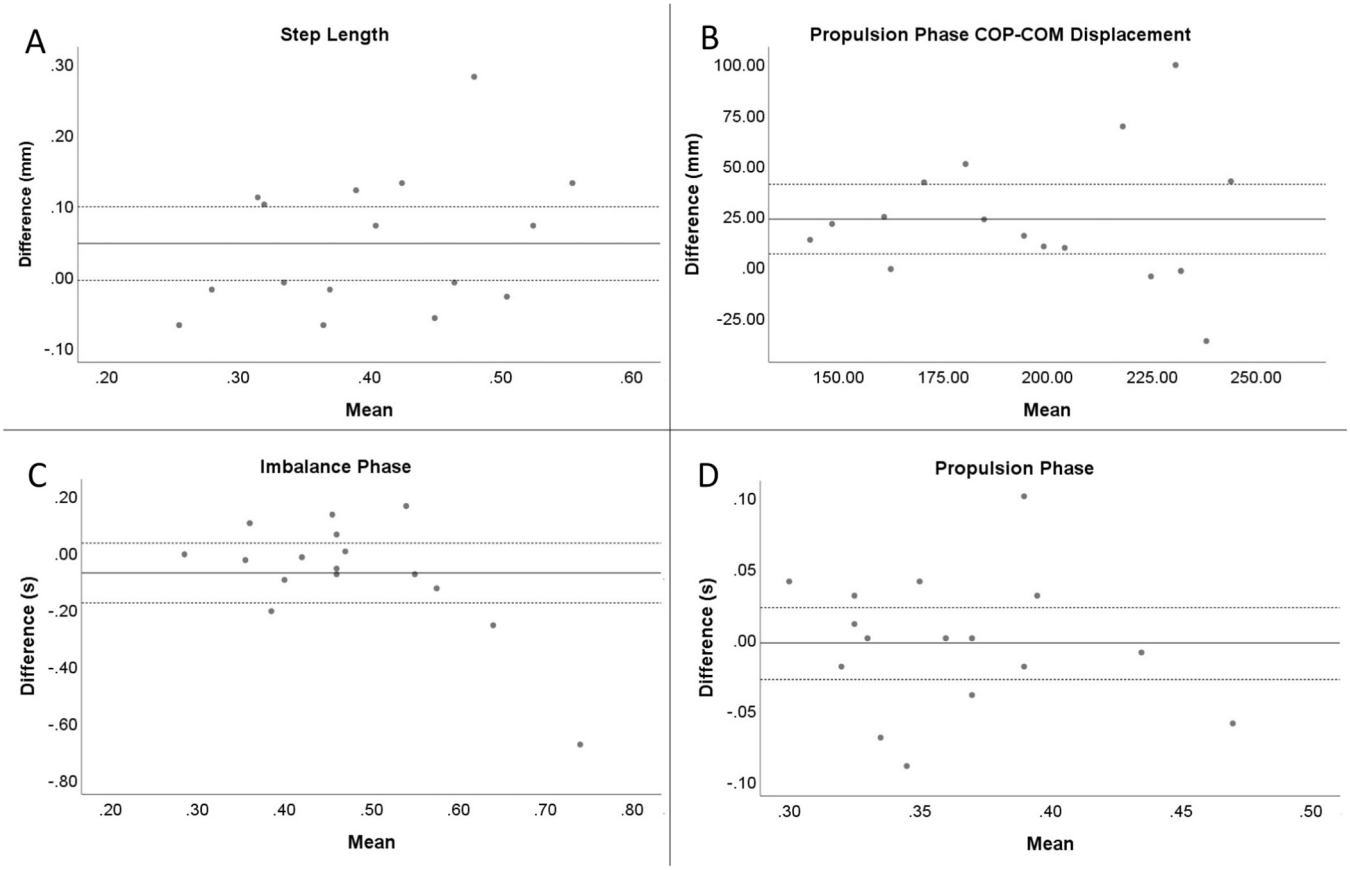

Fig. 2. Bland-Altman plots of between-session differences (On vs. Off medication) plotted against mean values for selected spatiotemporal measures of gait initiation in 16 persons with Parkinson's disease. Solid lines indicate the average mean difference; dotted lines delineate the 95% confidence interval. No systematic variances in group performance between distinct medication conditions in A, C, and D. Systematic variance is noted in group performance in B. Uniform relationships between the different medication conditions and the mean performance are seen (A, B, D) while a nonuniform relationship (proportional bias) is noted in C.

4. Discussion

The purpose of this study was to identify the reproducibility and responsiveness of spatiotemporal measures of GI from three-dimensional analysis of kinetic and kinematic variables in persons with PD. Our results suggest that most measures of GI can reliably be used to assess GI in persons with PD, whether they are On or Off-medication.

4.1. Relative reliability

The ICCs from the present study were good-to-excellent (0.66–0.960) for most of the spatiotemporal measures of GI, with an overall range of 0.417–0.960. A discussion of these findings relative to other studies can be found in Appendix G.

4.2. Absolute reliability

The SEM and %SEM were used to represent the smallest amount of change necessary to indicate real change (beyond measurement error) for a group of subjects. In the present study %SEM values were all low (<30%), with the range between 3.39% and 27.35% for all variables. Absolute reliability was higher in participants when On medication compared to Off medication, in all variables except for CoP-CoM displacements. A discussion of the absolute reliability of CoP-CoM displacements when assessed On medication can be found in Appendix H.

4.3. Responsiveness

Most outcome measures (12/16) require low-to-moderate amounts of change (<50%) to indicate true change (beyond measurement error) in individual participants. The presence or absence of dopamine replacement medication had little effect on responsiveness. The mean %MDC values for spatiotemporal measures assessed On medication was 37.9% compared to 40.8% when assessed Off medication. Researchers can take confidence using spatiotemporal measures to identify real change in GI performance for patients with PD regardless of their present medication condition.

4.4. Reliability of assessments during on vs off medication conditions

The relative reliability of repeated measurements was strongest when participants were tested Off medication (ICC range 0.783–0.945). In contrast, the absolute reliability of repeated measurements was greatest when participants were tested On medication (%SEM < 25%). The apparent contradiction in assessments of reliability can be explained by the comparatively large standard deviations seen when participants were repeatedly assessed Off medication. This suggests that clinicians might consider performing assessments of PD patients during both On and Off medication periods (Foreman et al., 2011). For a further discussion on the merits of assessing GI On and Off medication, see Appendix I.

4.5. Limitations

First, there are numerous spatiotemporal outcome measures in the three-dimensional assessment of GI but our results should not be generalized beyond the variables specifically assessed here. Second, our results may not be applicable for persons with greater severity of PD, or those receiving medical care beyond standard dopamine replacement (e.g., Deep Brain Stimulation). Finally, our sample size was relatively small (n = 16) and we recognize that this might affect our ability to accurately reflect population means with this data.

5. Conclusions

Based on our knowledge, this is the first study to examine the reliability and reproducibility of spatiotemporal kinetic and kinematic outcomes of GI from three-dimensional systems in persons with PD. These results suggest that spatiotemporal outcome measures of GI using motion capture technology are highly reliable and responsive to changes in performance for persons with mild-to-moderate PD.

Conflict of interest statement

Declarations of interest: none.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jbiomech.2019.03.009.

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