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Quantifying turning behavior and gait in Parkinson's disease using mobile technology

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ABSTRACT

Gait and balance impairments associated with Parkinson's disease (PD) are often refractory to traditional treatments. Objective, quantitative analysis of gait patterns is crucial in successful management of these symptoms. This project aimed to 1) determine if biomechanical metrics from a mobile device inertial measurement unit were sensitive enough to characterize the effects of anti-parkinsonian medication during the Timed Up and Go (TUG) Test, and 2) develop the Cleveland Clinic Mobility and Balance application (CC-MB) to provide clinicians with objective report following completion of the TUG. The CC-MB captured 3-dimensional acceleration and rotational data from people with PD (pwPD) to characterize center of mass movement while performing the TUG. Trials were segmented into four components: Sit-to-Walk, Gait, Turning, and Stand-to-Sit. Thirty pwPD were tested On and Off (12 h) anti-PD medication. Significant improvements ($p < 0.05$) between On versus Off conditions included: reduction in MDS-UPDRS III motor scores (10.7%), faster trial times (9.3%), more dynamic walking as evident by increased normalized jerk scores (vertical: 17.3%, medial-lateral: 12.3%), shorter turn durations (10.4%), and faster turn velocities (8%). Measures in Sit-to-Walk and Stand-to-Sit did not show significant changes. Trial time and turn velocity showed excellent test-retest reliability (ICC range: 0.83-0.96) across both medication states. A mobile device platform provided quantitative measures of gait and turning during the TUG that detected significant improvements from anti-parkinsonian medications. This platform is a low-cost, easy-to-use tool that can provide objective reports immediately following the clinical assessments, making it ideal for use in and outside the clinical setting.

Introduction

Parkinson's disease (PD) is a neurodegenerative disease that is associated with debilitating gait and/or postural impairments (Mellone et al., 2016; Zampieri et al., 2011; Weiss et al., 2011) that are often refractory to pharmaceutical (McNeely and Earhart, 2011; Curtze et al., 2015) and surgical treatment (St George et al., 2010) approaches. Seventy-seven percent of people with PD (pwPD) will develop gait and postural instability (Kang et al., 2005), and it is estimated that 60% of pwPD will experience a fall (Allen et al., 2013). Despite such high fall rates, clinicians do not currently have an objective and reliable method for characterizing fall risk in PD. In fact, the best predictor of falls in PD is the occurrence of a fall in the preceding year (Nocera et al., 2013). Improving the effectiveness of treatment for gait and postural instability requires reliable and objective measures that accurately capture the severity of such impairments.

The Timed Up and Go Test (TUG) may be the most widely used clinical test of functional mobility in neurological and geriatric populations (Mancini and Horak, 2010). The TUG requires the subject to stand from a seated position in a chair, walk 3 m, turn, walk back to chair, turn and sit (Mathias et al., 1986). The TUG is valid (Brusse et al., 2005) and reliable (Huang et al., 2011) in the PD population and traditionally, performance is based on total time to complete the task. One limitation to total time as the outcome metric for the TUG is that it collapses the total performance during the trial into one measure and therefore lacks the resolution to determine the performance of the individual components: Sit-to-Stand, Gait, Turn, and Turn-to-Sit.

Wearable sensors, accelerometers and gyroscopes have provided objective, portable biomechanical measures of movement at a modest cost (Mancini and Horak, 2010; Salarian et al., 2010; Zampieri et al.,

Abbreviations: AP, anterior-posterior; CC-MB, Clinic Mobility and Balance Application; cvCadence, coefficient of variation for cadence; ICC, IntraClass Correlation Coefficient; IMU, inertial monitoring unit; ML, medial-lateral; NJS, Normalized jerk scores; PD, Parkinson's disease; pwPD, people with Parkinson's disease; RMS, root mean square; STW, Sit-to-Walk; TTS, Turn-to-Sit; TUG, Timed-Up-And-Go-Test; V, vertical

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2010; Salarian et al., 2009; Palmerini et al., 2013). Recently, Salarian and colleagues reported no difference in total time to complete the TUG when comparing pwPD to their healthy peers; however, a multi-unit body sensory system detected decreased cadence during walking, increased turn time, and increased turn-to-sit time in the pwPD (Salarian et al., 2010). Ponti and colleagues used a single accelerometer (Ponti et al., 2017) and reported that overall time did not differentiate between fallers and non-fallers in healthy older adults; however, a frequency analysis of the TUG components was able to discriminate between the two groups.

Although systems do exist on the market which use accelerometers and gyroscopes to provide a portable system for instrumenting the TUG (McGrath et al., 2011; Greene et al., 2014a,b; Mancini et al., 2011), the process from collecting data to generating an easily-understood clinical report based on biomechanical measures of the components of the TUG can still be a multi-step process. Considering most clinical environments have established clinical workflows, a need exists for a simple, yet valid, approach to quantifying functional gait performance. A native inertial monitoring unit (IMU) coupled with an application on a commercially available mobile device platform has the potential to serve as an all-inclusive system for data collection, data storage, data processing, and report generation (Ozinga and Alberts, 2014; Ozinga et al., 2017) that is simple to use and has potential for integration into clinical workflows. The use of such a device in TUG assessments would allow for test administrators with varying levels of technical skills to generate quantitative assessments predicated on biomechanical metrics, via a portable, simple-to-use system in practically any environment providing more real-world metrics to base clinical decisions. This project aimed to 1) detect differences in performance On and Off medication within the individual components of the TUG in pwPD, and 2) develop a mobile device application, the Cleveland Clinic–Mobility and Balance application (CC-MB) that could provide an objective report following the assessment.

Experimental procedures

Participants

Thirty subjects (12 females/18 males; 61.9 ± 9.0 years) diagnosed with idiopathic PD were recruited from the Center for Neurological Restoration within the Cleveland Clinic. A detailed study protocol has been described previously (Rosenfeldt et al., 2015). Inclusion criteria were: clinical diagnosis of idiopathic PD, between 30 and 75 years of age, not currently engaged in physical therapy for their PD or another interventional clinical study, Hoehn and Yahr stage II-III while on antiparkinsonian medication. Primary exclusion criteria include: presence of dementia, previous stroke, any medical or musculoskeletal contraindications to exercise, and existing cardiorespiratory disease. Subjects provided written consent, the Cleveland Clinic Institutional Review Board approved this study, and all procedures were in accordance with the 1964 Helsinki declaration and its later amendments. Subjects were tested on two separate days (randomized): one day on their regular dose of antiparkinsonian medication and the other off medication for a minimum of 12 h prior to testing. For all participants, the mean disease duration was 4.0 ± 3.0 years, 25/30 pwPD were in Hohen & Yahr stage 2.5 or lower, and Levodopa Equivalent Daily Dose for the group was 513.1 ± 256 mg.

Experimental protocol

Prior to testing, an iPad®(Cupertino, CA) mobile device was secured to the subject's lumbar spine in a vertical position to approximate whole body center of mass (Ozinga and Alberts, 2014; Ozinga et al., 2017). A custom-made band was used to secure the iPad to accommodate for differences in body types. The TUG was performed in a carpeted hallway, where subjects sat on the front edge of an armless chair to begin the trial. Upon hearing the auditory cue from the CC-MB application, the subject was instructed to stand up from the chair, walk to a traffic cone positioned 3 m away, make a 180° turn, walk back to the chair, turn and sit. Each subject completed two trials per medication state. A rest period was given when needed.

Data acquisition and analysis

A custom application for the mobile device platform (CC-MB) was created to acquire and store 3D accelerometer (ST Micro LIS331DLH) and 3D gyroscope (ST Micro L3G4200D) data from the embedded sensors in the mobile device during the task (Ozinga and Alberts, 2014). Data were sampled at 100 Hz. Device specification and details on data storage have been described previously (Ozinga and Alberts, 2014). To develop the CC-MB, the administrator extracted the data from the tablet following test completion. Data were securely transmitted to a HIPPA compliant research database for off-line data analysis in MATLAB (TheMathWorks, Inc.) and development of the algorithm. Once the algorithm was established and tested to determine its ability to discriminate TUG performance across medication states, the algorithm was written in C to validate that all aspects of the algorithm can be utilized for on-board processing of the trials on the mobile device in future projects.

The acceleration signal utilized in the analyses of this manuscript was the 'userAcceleration' signal which is directly exported from the iPad (Apple CMDeviceMotion, 2018). Specifically, proprietary algorithms are used to separate the acceleration of the device due to forces exerted by the user and forces due to gravity, and both can be exported from the iPad. The exported 'userAcceleration data' and the gyroscope data measure motion with respect to an internal 3-dimensional, orthogonal, right-handed coordinate system. Although care was taken to position the iPad in the same orientation on all trials, small deviations in positioning the device could lead to erroneous results when data is compared across trials. To avoid this, the first 10 samples of the gravitational acceleration data from each trial were used to construct an inertial 3-dimensional orthogonal coordinate system where the acceleration due to gravity was only measured in one axis (vertical) via direction cosine matrix calculations (Tundo, 2013). For each trial, the measurements of the iPad sensors were transformed to an inertial coordinate system through the use of the direction cosine matrix which standardized the measurements across patients and trials. These transformed measurements are the outcomes reported in this study.

Each trial was segmented into the five components: Sit-to-Walk (STW), Gait Ascend, Turn, Gait Descend, and Turn-to-Sit (TTS) (Fig. 1b) using the linear acceleration and angular velocity in the anterior-posterior (AP), medial-lateral (ML) and vertical (V) direction in conjunction with previously reported methods adjusted with data specific parameters. Specifically, AP acceleration data were used to determine the gait initiation time point, and to separate the STW and Gait Ascend phases. Initial foot contact during the forward walking (i.e. gait initiation) was defined as the first forward motion peak of the filtered AP acceleration data greater than 0.5 m/s^2 that occurred preceding a change in sign (Zijlstra and Hof, 2003). A low-pass, 20 Hz zero-lag 4th order Butterworth filter was applied. Onset and offset of turning was determined using a theoretical model of walking and 180° turning motion which was fit to the angular position data (V) using a least squares optimization algorithm that determined the onset and offset time point of turns and has been previously validated (Salarian et al., 2009). Specifically, angular velocity data from the gyroscrope was bandpass filtered using a zero-lag 4th order Butterworth filter with cutoff frequencies of 0.25 Hz and 20 Hz. Once filtered, the angular position was calculated from the angular velocity data using the approximation of the cumulative integral via the trapezoidal method (MATLAB R2016). The mathematical model for turning fit a line with three segments: first line segment was a horizontal line, second line segment had a constant slope, third line segment was a horizontal line,

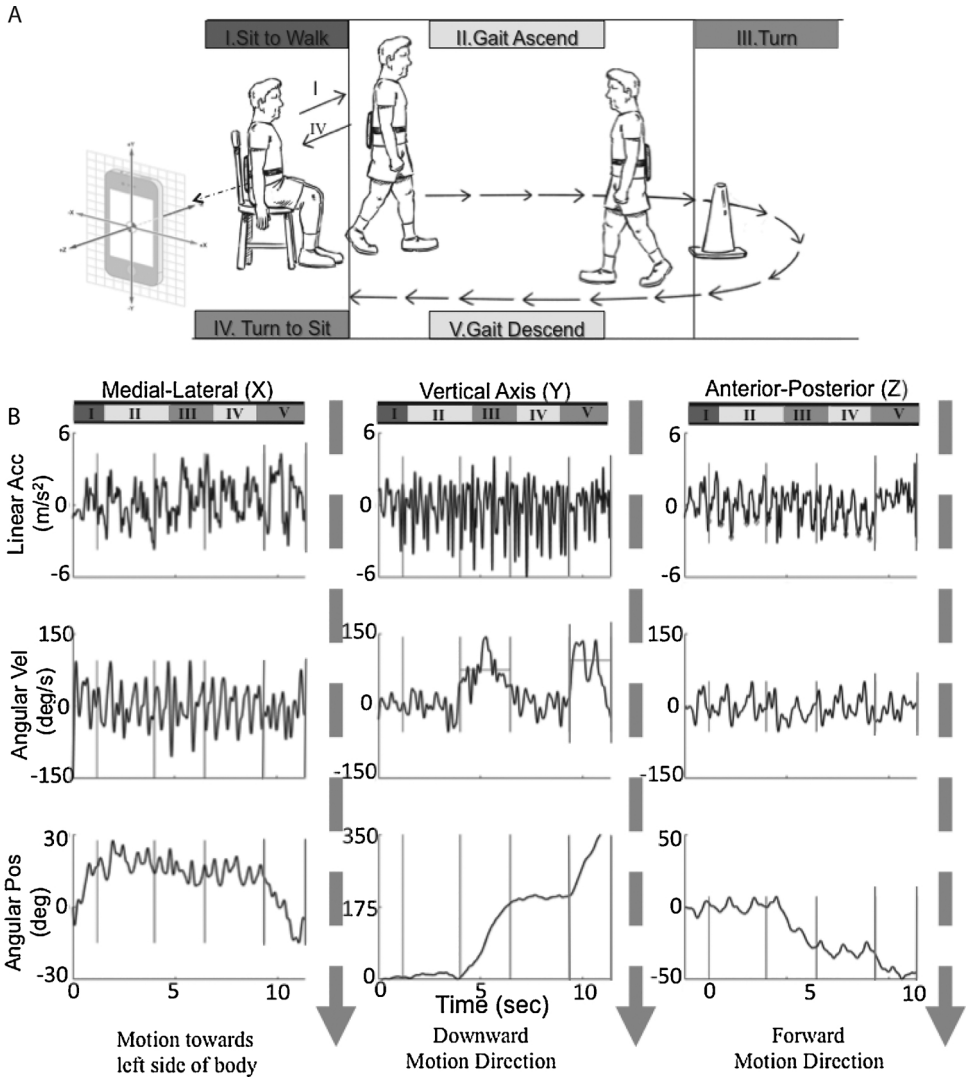

Fig. 1. a) Experimental protocol and components of the TUG. b) Raw data from the iPad's IMU sensors collected from a representative pwPD performing one trial of the TUG. The numbered bars located on the top row of the graphs show the duration of the components of the TUG that were detected by the algorithm: I) Sit-to-Walk, II) Gait Ascend, III) Turn, IV) Gait Descend, and V) Turn-to-Sit.

via a least squares optimization algorithm. The transition points from zero slope to constant slope were used to mark the onset and offset of the turns. Gait Ascend and Descend were segmented automatically through the aforementioned analyses. Foot contacts during the gait intervals were defined as peaks in the filtered (low pass zero lag, 20 Hz, 4th order Butterworth Filter) anterior acceleration (Zijlstra and Hof, 2003).

The kinematic outcome metrics for this study were a subset of measures that were shown to differentiate between TUG in early stage PD Off medications compared to age-matched healthy controls (Zampieri et al., 2011; Salarian et al., 2010; Zampieri et al., 2010; Palmerini et al., 2013) and were calculated via methods listed in the articles referenced with each metric. Gait metrics were calculated for Gait Ascend and Descend components in one trial (Fig. 1a) and averaged to produce one value per trial, defined as Gait measures. Metrics for Sit-to-Walk, Gait, Turning, Turn-to-Sit, and Total Trial components included: Time duration (sec), root mean square of linear acceleration (RMS) (m/s^2) (Palmerini et al., 2013) in AP, ML and V. Additional gait measures include cadence (steps/min) (Salarian et al., 2010) using previously defined method for identifying foot contact (Zijlstra and Hof, 2003) and the coefficient of variation for cadence (cvCadence) (unitless) (Palmerini et al., 2013). Normalized jerk scores (NJS) of acceleration were calculated for all TUG components. For calculation of the NJS, the acceleration data was bandpass filtered with a 4th order zero-lag Butterworth filter with cutoff frequencies of 0.15 and 5 Hz (Palmerini et al., 2013). For gait, the NJS (m) was calculated using the time duration between each foot contact using the Gait NJS equation in (Palmerini et al., 2013) which states:

$$Gait\ NJS = \frac{1}{N}\sum_{i=1}^{N}\sqrt{\frac{(hs_{i+1}-hs_i)^5}{2}\int_{hs_i}^{hs_{i+1}}(\dot{a})^2 dt} \quad (1)$$

where hs_i represents the time of the ith heel strike and a is the acceleration in m/s^2.

For all other TUG components, the time duration of the segment was used as the measure of time in the equation (Palmerini et al., 2013), and the NJS equation reduced to:

$$NJS = \sqrt{\frac{T^5}{2}\int_{Tstart}^{Tend}(\dot{a})^2 dt} \quad (2)$$

where T is the time duration in seconds (Tend-Tstart) of the each TUG phase and a is the acceleration measured in m/s^2.

Turning measures included: average turning velocity and peak velocity (deg/s) (Salarian et al., 2010; Zampieri et al., 2010; Salarian et al., 2009). The outcome measures were calculated for each trial and

averaged within a medication state per pwPD to yield one outcome measure for the On and Off evaluations.

The Movement Disorders Unified Parkinson's Disease Rating Scale motor score (MDS-UPDRS-III), a clinical test of motor symptoms, was evaluated by the same blinded clinical rater On and Off medication during the same testing visit as the TUG.

Statistical analysis

A paired *t*-test or a Wilcoxon Sign Rank test was used based on the distribution of the data to determine significant differences between the On and Off medication trials in clinical and quantitative measures. The average adjusted coefficient of determination (R^2) across all trials was used to evaluate the quality of fit between the mathematical model for turning and the angular position (V) data (Salarian et al., 2009). A correlation analysis, Spearman Rank or Pearson Moment Product, was performed between the clinical scores, MDS-UPDRS-III, and quantitative metrics to determine if a significant relationship existed. Test-retest reliability was assessed for both the On and Off medication conditions separately using the IntraClass Correlation Coefficient (ICC) (Koo and Li, 2016). The ICC(3,1) was used to assess test-retest reliability of a single medication state because the same device was used for each subject during all trials (Ozinga and Alberts, 2014). ICC values were classified as: 0.4 (poor reliability), 0.4–0.75 (fair to good reliability), and greater than 0.75 (excellent reliability) (Rosner, 2010).

Results

Average On medication total trial times measured by the CC-MB app were significantly faster (9.3%, $p = 0.01$, Table 1) compared to Off medication times for the entire group. The MDS-UPDRS-III motor scores demonstrated a significant improvement (10.7%, $p = 0 < 0.01$) On medication compared to Off (36.1 ± 9.8 and 40.4 ± 10.7 points, respectively).

Using sensor data from the mobile device, the algorithms automatically detected the five components of the TUG during each trial. Fig. 2 displays sensor data from a representative pwPD in the On and Off medication state.

Visual inspection of the two figures indicates that the pwPD completed the task 2.5 s faster when On compared to Off medication, with all five phases displaying a longer duration Off compared to the On medication state. In addition, Fig. 2a–b highlights the acceleration in the anterior direction (negative values due to the orientation of the iPad on the subject's back) having larger peak amplitudes and a larger range of values in the On compared to Off condition, indicating more dynamic motion in both the anterior and posterior directions. Fig. 2c–d shows the angular velocity about the vertical axis from the gyroscope sensor of the IMU. During turning, the average velocity On medication is faster compared to Off. Fig. 2e–f displays the rotational motion about the vertical axis and highlights the increased duration during Turning in the Off versus On medication states, and also illustrates similar movement patterns/strategies that were utilized with respect to turning.

Similar trends were evident in the group analysis. The NJS during Gait increased in two of the three directions (V and ML axes, Table 1). The vertical axis showed an increase of 17.3% ($p = 0.01$) from Off to On medication conditions and the ML direction increased by 12.3% ($p = 0.03$). Turn duration was significantly faster by 10.4% ($p = 0.02$) and average turn velocity increased by 8% ($p = 0.01$) in the On compared to Off medication condition. The coefficient of determination (R^2) was used as a measure of goodness of fit between the raw turning data and the mathematical model of turning, and on average, the two were closely aligned across all 120 trials (average $R^2 = 0.99$).

Average total trial time in the Off medication state did not show a significant relationship with disease severity measured via the MDS-UPDRS-III Motor Score in the Off medication state ($p = 0.20$). Percent improvement in the NJS (V) measures On and Off medication were positively correlated with the percent improvement in the MDS-UPDRS-III scores (rho = 0.41, $p = 0.025$).

Total trial time quantified by the CC-MB application exhibited the highest test-retest reliability between the On and Off medication states, (ICC/On = 0.96; ICC/Off = 0.90). The average turn velocity metric had an ICC of ICC/Off = 0.83; [0.67,0.91] in the Off medication state and an ICC of 0.85; [0.71,0.93] in the On state. Additional metrics from the Gait component also had good test-retest reliability, however the Sit-to-Walk metrics showed the lowest (Table 1).

Discussion

This study has demonstrated, for the first time, that the native IMU sensor coupled with an application on a mobile device platform was able to detect differences in total trial time, gait, and turning performance in pwPD between On and Off medication conditions. Multiple studies in PD have documented the importance of assessing the individual subtasks of TUG (Weiss et al., 2011; Salarian et al., 2010; Zampieri et al., 2010; Palmerini et al., 2013), through the use of motion capture systems, accelerometers and gyroscopes, and/or with video. While such laboratory assessments serve to improve our understanding of the declining performances of pwPD during certain components of the TUG, they are not always assessable due to cost and expertise needed in data collection, analysis, and interpretation, limiting their adoptability in the clinical workflow. The mobile device platform utilized in this study can serve as an all-in-one tool in which raw IMU sensor data can be converted to summary metrics quantifying gait, turning, and weight transfer performances in addition to timing measures, providing an immediate and comprehensive assessment of a person's performance during the TUG. Test administrators, regardless of technical expertise, can generate an objective quantitative assessment of postural and gait performances using a low-cost, easy-to-use device.

The finding that pwPD completed trials significantly faster (Table 1) On medication versus Off supports previous results showing that medication improves movement speeds in mild to moderate PD (Auriel et al., 2006; Ben-Itzhak et al., 2008). Average total trial time for pwPD in this study On to Off medication (7.4 ± 1.7 s to 8.2 ± 1.9 s, respectively) was faster than previously reported values for PD fallers (12.2 ± 7.42 to 15.5 ± 11.03) (Foreman et al., 2011),but comparable to times from PD non-faller times (8.13 ± 2.34 to 7.94 ± 2.15) (Foreman et al., 2011), suggesting this subject population exhibited a mild disease state and/or were not fallers.

The significant improvement from medication on the average MDS-UPDRS-III scores (decrease of 4.0 points On versus Off medication), exceeded the minimal clinically important difference of a decrease of 3.25 points (Horvath et al., 2015), and provides evidence that this group was indeed responsive to dopaminergic medication. Average total trial time Off medication was not significantly correlated with disease severity as measured by the MDS-UPDRS-III motor score Off medication, and given the large range of symptoms encompassed by the MDS-UPDRS-III motor score, this finding seems reasonable. Mancini et al. demonstrated that biomechanical measures of postural stability worsened over a 12 month period in pwPD that were de novo to anti-PD medications while UPDRS-III scores remained stable (Mancini et al., 2012); thus demonstrating the need for biomechanical measures to capture more sensitive measures of disease progression.

Gait

Measurements from the IMU sensors indicated that subjects On medication walked with a higher NJS in the V and ML directions compared to Off. The NJS during gait measures the time normalized rate of change in the acceleration signal during stepping, thus a fast and large variations in the time series data led to large values in the metric (Palmerini et al., 2013). During a typical gait cycle the center of mass translates in the direction of motion, but also moves in a sinusoidal

Table 1
TUG summary metrics calculated from IMU sensor data in Off and On medication states. Bolded values indicated a significant improvement ($p < 0.05$) from Off Meds to On Meds.

	Off Meds		On Meds		
	Mean (SD) *Median (IQR)	ICC (3,1) [LB-UB]	Mean (SD) *Median (IQR)	ICC (3,1) [LB-UB]	P Value
Time					
Total Time (s)	**8.19 (2.31)***	**0.96 [0.92 0.98]**	**7.43 (1.90)***	**0.90 [0.81 0.95]**	**0.01**
Sit-to-Stand (s)	0.76 (0.29)*	0.29 [−0.06 0.06]	0.71 (0.42)*	0.60 [0.32 0.79]	0.59
Gait (s)	3.68 (0.83)*	0.83 [0.67 0.91]	3.53 (0.53)*	0.54 [0.23 0.75]	0.85
Turn (s)	**1.54 (0.40)***	0.69 [0.45 0.84]	**1.38 (0.54)***	**0.80 [0.63 0.90]**	**0.02**
Turn to Sit (s)	1.76 (0.74)*	0.91 [0.82 0.95]	1.80 (0.66)*	0.82 [0.67 0.91]	0.24
Sit-to-Walk					
RMS ML (m/s^2)	1.54 (0.71)	0.64 [0.37 0.81]	1.69 (0.72)	0.59 [0.31 0.78]	0.17
RMS V (m/s^2)	1.83 (0.96)*	0.69 [0.45 0.84]	1.87 (0.74)*	0.70 [0.46 0.84]	0.46
RMS AP (m/s^2)	1.84 (1.2)*	0.76 [0.55 0.87]	1.99 (0.73)*	0.67 [0.41 0.82]	0.19
NJS ML (m)	4.05 (4.7)*	0.1 [−0.26 0.43]	4.03 (4.4)*	0.27 [−0.08 0.57]	0.88
NJS V (m)	6.51 (7.01)*	0.06 [−0.3 0.40]	6.57 (7.73)*	0.53 [0.23 0.74]	0.83
NJS AP (m)	4.3 (4.89)*	0.12 [−0.23 0.45]	4.93 (5.92)*	0.48 [0.16 0.71]	0.98
Gait					
RMS ML (m/s^2)	1.97 (1.01)*	0.94 [0.89 0.97]	2.11 (0.99)*	0.87 [0.74 0.93]	0.30
RMS V (m/s^2)	2.08 (1.13)*	0.92 [0.84 0.96]	2.25 (0.69)*	0.89 [0.78 0.94]	0.17
RMS AP (m/s^2)	2.27 (1.33)*	0.90 [0.8 0.95]	2.58 (1.00)*	0.82 [0.67 0.91]	0.19
NJS ML (m)	**5.72 (1.42)***	**0.61 [0.33 0.79]**	**6.42 (3.67)***	**0.76 [0.56 0.88]**	**0.03**
NJS V (m)	**5.16 (1.62)**	**0.73 [0.51 0.86]**	**6.05 (1.94)**	**0.79 [0.61 0.89]**	**< 0.01**
NJS AP (m)	6.68 (2.85)*	0.73 [0.52 0.86]	6.75 (4.50)*	0.72 [0.49 0.85]	0.06
Cadence(steps/min)	126.42 (20.65)	0.75 [0.54 0.87]	123.0 (18.46)	0.81 [0.64 0.90]	0.11
cvCadence	0.05 (0.06)*	0.65 [0.39 0.81]	0.04 (0.04)*	0.53 [0.23 0.75]	0.58
Turning					
RMS ML (m/s^2)	2.14 (1.04)*	0.89 [0.78 0.94]	2.39 (0.93)*	0.83 [0.68 0.91]	0.24
RMS V (m/s^2)	1.84 (0.62)	0.71 [0.47 0.85]	1.88 (0.55)	0.80 [0.63 0.90]	0.64
RMS AP (m/s^2)	2.05 (1.25)*	0.90 [0.81 0.95]	2.26 (0.73)*	0.83 [0.68 0.91]	0.26
NJS ML (m)	43.35 (21.04)*	0.80 [0.62 0.90]	32.55 (29.05)*	0.78 [0.60 0.89]	0.05
NJS V (m)	46.21 (55.36)*	0.58 [0.29 0.77]	33.89 (40.13)*	0.80 [0.63 0.90]	0.10
NJS AP (m)	45.56 (28.97)*	0.74 [0.52 0.86]	39.26 (47.00)*	0.72 [0.49 0.85]	0.13
Average Velocity (deg/s)	**90.94 (15.20)**	**0.83 [0.67 0.91]**	**98.19 (20.24)**	**0.85 [0.71 0.93]**	**0.01**
Peak Velocity (deg/s)	163.66 (41.25)	**0.84 [0.69 0.92]**	172.73 (39.71)	0.80 [0.62 0.90]	0.14
Turn-to-Sit					
RMS ML (m/s^2)	1.80 (0.83)*	0.82 [0.66 0.91]	1.74 (0.70)*	0.86 [0.73 0.93]	0.86
RMS V (m/s^2)	1.40 (0.79)*	0.70 [0.47 0.84]	1.43 (0.69)*	0.89 [0.79 0.95]	0.53
RMS AP (m/s^2)	1.52 (0.90)*	0.80 [0.63 0.91]	1.76 (0.72)*	0.90 [0.81 0.95]	0.06
NJS ML (m)	56.40 (39.8)*	0.92 [0.85 0.96]	58.09 (61.27)*	0.74 [0.53 0.87]	0.21
NJS V (m)	60.23 (68.22)*	0.87 [0.75 0.94]	65.13 (37.39)*	0.70 [0.47 0.84]	0.40
NJS AP (m)	61.60 (54.31)*	0.75 [0.54 0.87]	55.84 (51.37)*	0.74 [0.53 0.87]	0.62

pattern in the vertical and lateral directions (Orendurff et al., 2004). Previous studies have shown that NJS are lower in PD compared to healthy controls (Palmerini et al., 2013) in the ML and AP direction during walking and suggest that the decreased NJS values in PD was a reflection of a general loss of complexity of the motor control system, likely due to bradykinesia which inhibits movements with fast and large variations. Hence, in gait, increases in NJS correlated with increase in dynamic stepping which may reflect a more typical sinusoidal pattern of healthy controls. This study and one other (Palmerini et al., 2013) found excellent test-retest reliability of NJS in both medication states. Taken together, these results support using the NJS metric to detect gait impairments in pwPD.

Although the RMS of acceleration increased with medication across all three directions (Table 1), these increases were not significant. The lack of significant improvement in the RMS in contrast to the NJS, could indicate that although subjects exhibit a large range of acceleration, it is the rate of change that is significant. Palmerini et al. found that the RMS during the gait portion of the TUG was not significant or reliable (Palmerini et al., 2013). Further work is needed to determine the merit of using RMS of acceleration for quantifying balance and gait in pwPD.

In this study, neither cadence nor the variability of cadence showed a significant change between On and Off medication even though trial time was significantly decreased. This result is supported by a previous study which found that while gait velocity increased in pwPD On medication compared to Off, other qualitative measures of gait such as step frequency (step/min) and double limb support time did not change (Elshehabi et al., 2016). The authors suggested that the disparity of improvement between gait speed and measures of gait and variability of gait performance may demonstrate instability and increased fall risk (Boonstra et al., 2008). It is also possible that the three meter distance used during the TUG is not far enough to detect changes in cadence and step length, as other studies have suggested moving to a testing protocol that incorporates a seven meter distance (Zampieri et al., 2010).

Turning

Consistent with other studies (McNeely and Earhart, 2011), medication improved the average turn velocity and duration by 8.0% and 10.4%, respectively. Turning assessments are critical for identifying postural instabilities as turning is more likely vulnerable to functional impairments (Macnini, 2015) because it is inherently asymmetrical and non-rhythmical and cannot stem from central pattern generators, unlike walking. Turning thus requires more attention and involves more inter-limb coordination compared to straight line walking (McNeely and Earhart, 2011). With turning being one of the most insightful tasks into postural instability and fall prediction, having a user-friendly device to objectively measure and report metrics that quantify turning performance could truly aide in posture and gait assessment in pwPD (King

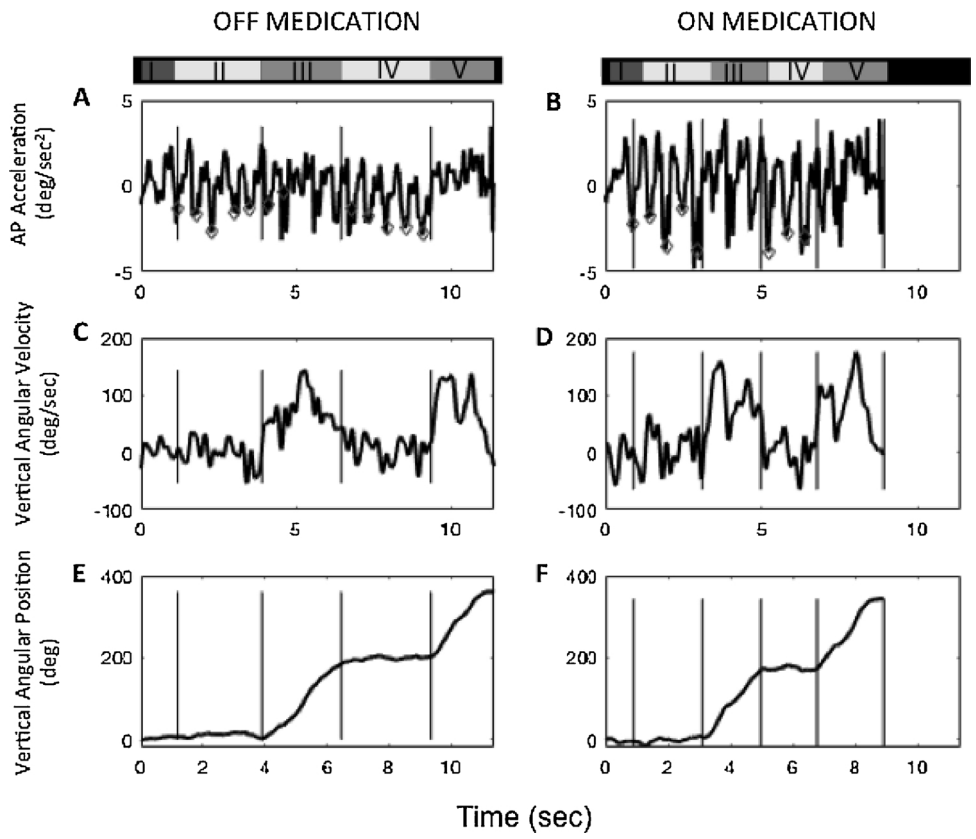

Fig. 2. A subset of IMU data from a representative pwPD in both the On and Off medication conditions. The numbered bars located on the top row of the graphs indicate the duration of the five components of the TUG. The diamonds in the graphs A-B indicate foot contact points.

et al., 2012; Herman et al., 2011).

Sit-to-Walk & Turn-to-Sit

Measures calculated during Sit-to-Walk and Turn-to-Sit subcomponents of the TUG were not significantly different between the On and Off-medication state. Few studies have analyzed the effects of medication during Sit-to-Walk and Turn-to-Sit behavior in pwPD. Palmerini showed that the RMS and NJS of acceleration and measures of duration for these subcomponents lacked the sensitivity to detect differences between controls and pwPD and reported some of lowest test-retest reliability of all the components of the TUG test (Palmerini et al., 2013), which could be related to the large variety of movements and postural strategies available to perform this activity (Salarian et al., 2010).

Limitations

The pwPD in this study were mildly impaired and therefore provided the necessary dynamic changes in the data for identification and segmentation of the TUG into the individual subcomponents for analysis. It is not known if the sensor system in the iPad could detect behaviors in a pwPD with more severe disease symptoms, including a shuffling gait or very slow turning behavior. While no participant complained of the iPad hindering their movements, it is unclear how the addition of the iPad to the lower back affected participant performance. This technology is transferable to an iPhone, and future studies can utilize a smaller device to perform the same analyses.

Conclusions

The CC-MB application on a mobile device platform can provide clinicians with a portable, accurate, simple-to-use system that can objectively and immediately quantify postural and gait stability with reliable biomechanical measures in pwPD. Using a single IMU in conjunction with the CC-MB application, we detected significant improvements from anti-PD medications in kinematic and timing measures during the Gait and Turning components of the TUG, that demonstrated excellent test-retest reliability while increasing objectivity for the assessment of mobility status.

Declarations of interest

None.

Author roles

All authors approve the final article. Research project: Conception: Mandy Miller Koop, Anson Rosenfeldt, Sarah Ozinga and Jay Alberts. Organization and Execution: Mandy Miller Koop, Sarah Ozinga, Anson Rosenfeldt, and Jay Alberts. Data Collection and Analysis: Mandy Miller Koop and Anson Rosenfeldt. Statistical Analysis: Design and Execution: Mandy Miller Koop and Statistical Analysis: Review and Critique: Jay Alberts. Manuscript Preparation: Writing of the first draft: Mandy Miller Koop and Anson Rosenfeldt. Manuscript Review and Critique: Mandy Miller Koop, Anson Rosenfeldt, Sarah Ozinga and Jay Alberts.

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