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Dopaminergic modulation of arm swing during gait among Parkinson's disease patients

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Abstract

Background—Reduced arm swing amplitude, symmetry, and coordination during gait have been reported in Parkinson's disease (PD), but the relationship between dopaminergic depletion and these upper limb gait changes remains unclear. This study investigated the effects of dopaminergic drugs on arm swing velocity, symmetry, and coordination in PD.

Methods—Forearm angular velocity was recorded in 16 PD and 17 control subjects (Controls) during free walking trials. Angular velocity amplitude of each arm, arm swing asymmetry, and maximum cross-correlation were compared between control and PD groups, and between OFF- and ON-medication states among PD subjects.

Results—Compared to Controls, PD subjects in the OFF-medication state exhibited lower angular velocity amplitude of the slower- ($p=0.0018$), but not faster- ($p=0.2801$) swinging arm. In addition, PD subjects demonstrated increased arm swing asymmetry ($p=0.0046$) and lower

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maximum cross-correlation ($p=0.0026$). Following dopaminergic treatment, angular velocity amplitude increased in the slower- ($p=0.0182$), but not faster- ($p=0.2312$) swinging arm among PD subjects. Furthermore, arm swing asymmetry decreased ($p=0.0386$), whereas maximum cross-correlation showed no change ($p=0.7436$). Pre-drug angular velocity amplitude of the slower-swinging arm was correlated inversely with the change in arm swing asymmetry ($R=-0.73824$, $p=0.0011$).

Conclusions—This study provides quantitative evidence that reduced arm swing and symmetry in PD can be modulated by dopaminergic replacement. The lack of modulations of bilateral arm coordination suggests that additional neurotransmitters may also be involved in arm swing changes in PD. Further studies are warranted to investigate the longitudinal trajectory of arm swing dynamics throughout PD progression.

Keywords

arm swing; dopamine; Parkinson's disease; locomotion; asymmetry; gait

1. Introduction

Parkinson's disease (PD) is a common neurodegenerative disorder marked pathologically by cell death of dopaminergic neurons in the substantia nigra pars compacta of the midbrain [1, 2]. Progressive nigral cell degeneration leads to dopamine depletion within the striatum and dysfunction of basal ganglia (BG) that is thought to be responsible for most of the classic clinical symptoms of PD patients (i.e. bradykinesia, rigidity, and tremor at rest) [3]. Gait dysfunction is recognized as the fourth cardinal sign of PD, manifested in advanced patients as freezing episodes or shuffling step pattern [4]. In addition to dopaminergic dysfunction, there is a growing recognition that extranigral, non-dopaminergic pathways may play a role in PD-related gait symptoms [5, 6]. For example, freezing of gait is known to be relatively unresponsive to dopaminergic treatment.

In the past, lower-limb gait dysfunction has been extensively studied and characterized [7, 8], whereas less is known regarding upper-limb gait dysfunction in PD. Lewek et al. [9] demonstrated recently that early-stage PD subjects exhibit marked arm swing asymmetry (ASA) while walking. Related research has highlighted upper-limb gait asymmetry and coordination deficits as a common and relatively early feature of PD [10–12]. Biomechanically, several lines of evidence suggest that impaired arm swing may arise from wrongly timed activation of the shoulder flexors or extensors [13], axial rigidity [14, 15], and/or loss of trunk rotation during ambulation [16–18]. The relationship between dopamine deficits and these upper-limb gait changes in PD, however, remain unknown.

Several lines of evidence support the notion that nigrostriatal dopaminergic loss plays a role in the etiology of upper-limb gait dysfunction in PD. First, using [^{123}I] N- ω -fluoropropyl-2 β -carbomethoxy-3 β -(4-iodophenyl)-tropane (FP-CIT) and single-photon computed tomography, Isaías et al. [19] reported that asymmetric dopaminergic terminal labeling in the striatum correlates strongly with upper-limb gait asymmetry in PD subjects. Second, combined dopaminergic medication and bilateral subthalamic nucleus (STN)

stimulation have been shown to ameliorate reduced walking arm swing amplitude among PD patients [16, 17].

In this study, we aimed to characterize the effects of acute dopaminergic therapy on upper limb gait in PD. We utilized triaxial inertial motion sensors to measure the angular velocity of arm swing, and filtering to mitigate distal tremor artifacts (3–6 Hz) [20]. We hypothesized that arm swing angular velocities, symmetry, and bilateral coordination would improve following dopaminergic therapy among early-stage PD subjects.

2. Methods

2.1. Subjects

Sixteen PD subjects and 17 control subjects (Controls) (Table 1) were recruited from a tertiary movement disorders clinic with PD diagnosis confirmed by a movement disorders specialist using published criteria [21]. All were in relatively early disease stages [Hoehn and Yahr, stage (HY) 3], and able to walk unassisted. None of the subjects had other major medical conditions (e.g., cardiovascular, cancer, etc.), and they were negative for other neurological and psychological disorders, hypothyroidism, vitamin B₁₂ or folate deficiency, and kidney and liver disease. Disease duration was defined as time from first diagnosis of disease until the subject's participation in this. Unified PD Rating Scale part III (UPDRS-III) scores were obtained for each subject, and for PD subjects during both OFF- and ON-drug states. The OFF-drug state was defined as overnight dopaminergic drug withdrawal, and the ON-drug state as beginning approximately one hour after ingestion of PD medication [22]. Levodopa-equivalent daily dose (LEDD) was calculated according to published criteria [23]. The rigidity score for each subject was calculated as the mean of neck and right/left arm/leg rigidity scores from the UPDRS-III motor exam (items 3.3a–e). Tremor scores were calculated as the mean of the 10 tremor assessment items on the UPDRS-III motor exam (items 3.15–3.18). Most and least affected side for PD subjects was determined using side of first symptom onset, when available, and UPDRS-III scores. Written informed consent was obtained for each subject, in accordance with the Declaration of Helsinki. The research protocol was reviewed and approved by the Penn State Hershey Medical Center Institutional Review Board.

2.2. Arm swing data collection

Angular velocity of arm swing was recorded using wearable triaxial inertial sensors (APDM Emerald) secured to the wrists of each subject using an elastic strap similar to a wristwatch band. All subjects were instructed to walk at a comfortable pace around a 0.25-mile local track. We initially asked subjects to walk two laps (0.5 miles), but later found that many patients could only tolerate one lap or less. Subsequently, we asked subjects to complete one lap (0.25 miles), as tolerated (Table 1). PD subjects were instructed to walk both during OFF- and ON-drug states as described above. All subjects completed the trials without stopping or pausing. The angular velocities of each arm were sampled at 128 Hz, and the sensors were synchronized to align the recordings temporally.

2.3. Arm swing data preprocessing and normalization

The following steps were used to pre-process the raw arm swing data. First, the first and last five seconds of each trial were excluded from the analysis to remove artifacts introduced by initiation and termination of walking; Second, a low-pass (2 Hz) eighth-order Butterworth filter was applied to the triaxial data from each trial to remove higher-frequency (3–6 Hz) noise introduced by tremor [20]. Principal component analysis was used to obtain single-dimensional time series measurements from the triaxial sensor data. We originally attempted to account for differences in individual and left/right arm swing trajectories by calculating left and right principal components for each arm on a per-subject basis. The low swing amplitude of some PD subjects, however, yielded extremely unstable principal components due to the relatively higher variation across the lateral/medial directions and lower variation in the normal anterior/posterior direction. Instead, we used two (left and right) common principal components to establish a standardized reference direction for measuring angular velocity across all subjects. These common left and right principal components were derived using aggregate data from the control group, since these subjects had a greater amount of angular velocity variation in the normal (anterior/posterior) direction of arm swing. Specifically, the triaxial angular velocity recordings from all Controls first were truncated to match the length of the shortest trial, and then concatenated into a single vector. Principal component analysis (PCA) then was applied to the aggregate arm swing time series of the control subjects, yielding principal components of the left and right arms [24]. To register each recording to a common reference axis, the triaxial data from each subject then were projected onto the largest principal component of the left and right arms (Figure 1), respectively, yielding principal angular velocities $\omega_{L,i}$ and $\omega_{R,i}$ where $i = 1, 2, \dots, N$, with N being the total number of samples in the time series. All subsequent analyses were performed using these scalar values of angular velocity expressed along the left and right principal directions of arm swing.

2.4. Calculation of arm swing measurements (AVA, ASA, and MXC)

Angular velocity amplitude (AVA), arm swing asymmetry (ASA), and maximum cross-correlation (MXC) were derived from angular velocity measurements along the axis of the common left or right principle component for each arm (see above). Left and right AVA of each trial was derived using the root mean square amplitude of the projected angular velocity,

$$AVA = \sqrt{\frac{1}{N} \left(\sum_{i=1}^N \omega_i^2 \right)}$$

where N denotes the total number of samples within the trial and ω_i was the angular velocity at index i for either the left or right arm, as appropriate. For each subject, the greater and lesser AVA measurements between arms were used to identify “faster-swinging” and “slower-swinging” arms, respectively.

ASA was calculated for each trial by first computing the standard deviations of left and right angular velocities. The lesser of the two standard deviations was denoted $\sigma_{\min}$, and the

greater as $\sigma_{\max}$. ASA was derived using a variant of the general symmetry angle of Zifchock et al. [25]. Values of ASA range from 0 to 100. Higher values of ASA are indicative of greater asymmetry.

$$ASA = \frac{45^\circ - \arctan(\sigma_{\min}/\sigma_{\max})}{45^\circ} \times 100\%$$

For each trial, the normalized cross-correlation, $R_{LR}(k)$, at lag k , was defined as:

$$R_{LR}(k) = \frac{1}{\sigma_L \sigma_R} \left[\frac{1}{N-1} \sum_{i=0}^{N-k-1} \omega_{L,i+k} \omega_{R,i} \right]$$

where σ_L and σ_R were the standard deviations of angular velocity of the left and right time series, respectively. MXC was defined as the maximum absolute value of $R_{LR}(k)$, and indicates the degree of statistical dependence between right and left signals. The maximum absolute value of $R_{LR}(k)$ occurred at a lag k , where the value of k was typically within the range of zero $\pm$ one half arm swing period. The use of absolute value differs slightly from Huang et al. [10] by allowing for the negatively correlated phase of arm swing to be incorporated into MXC, in addition to the positively correlated phase. Accordingly, MXC was interpreted as a measure of inter-limb coordination. Also in contrast to Huang et al., angular velocity was used instead of angular acceleration, in order to provide a clinically intuitive metric of arm swing motion.

Within PD subjects, the change in each computed arm swing measurement (i.e., AVA of each arm, ASA, and MXC) were computed by subtracting the ON-medication value from the OFF-medication value ($\Delta X = X_{\text{OFF}} - X_{\text{ON}}$). “Faster-swinging” and “slower-swinging” arms of each subject were assigned according to high and low OFF-medication AVA scores, respectively.

2.5. Statistical analysis

Demographic and clinical parameters were compared between PD and Controls using two-sample Student's t -tests with pooled variance and Fisher's exact test. Age and duration of illness were evaluated as potential covariates in arm swing analyses, but these variables did not have significant associations with arm swing measurements. Thus, we did not include age and duration of illness as covariates in the arm swing analysis.

Group differences in ASA, AVA, and MXC, and motor scores were performed using two-tailed Wilcoxon Rank Sum tests with t -distribution approximation [26]. Within PD subjects, differences between OFF- and ON-drug arm swing measurements and UPDRS-III scores were assessed using the Wilcoxon Signed Rank test. The associations among arm swing measurements, LEDD, disease duration, UPDRS-III scores, and HY scores were explored using Spearman's rank correlation [27]. Correlations between arm swing measurements and clinical scores (i.e., UPDRS-III and HY scores) were adjusted for age and LEDD.

Contingency analyses (Table 1) were performed to determine whether distances walked during each trial were affected by disease or medication state. Each trial was categorized, respectively, as “long” if the subject walked the entire 0.5 miles or “short” if the subject walked less than 0.5 miles (Table 1). Chi-Square analysis was utilized to assess between-group (Control and PD OFF-medication) differences in trial length. McNemar’s test was used to assess for drug effects on trial length among PD subjects (OFF- and ON-medication states). All analyses were performed using SAS 9.3 (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Study subjects

Detailed demographic information is shown in Table 1. There were no significant differences between PD and Controls with respect to age ($p=0.3818$) or gender ($p=0.4905$). Among PD subjects, LEDD ranged from 250 to 1092 mg. There was a significant difference between OFF- and ON-drug UPDRS-III motor scores ($p=0.0016$). Duration of illness in the PD group ranged from 0.04 to 12.00 years. Trial distance (short/long) was not significantly different between disease statuses ($p=0.7283$) or medication states ($p=0.6072$).

3.2. Arm swing changes in PD and their modulation by dopaminergic drugs

Compared to Controls (Table 2), PD subjects (OFF-drug) demonstrated lower AVA of the slower-swinging arm ($p=0.0018$) and no difference for the faster-swinging arm ($p=0.2801$), higher ASA ($p=0.0046$), and lower MXC ($p=0.0026$). Figure 2 demonstrates the distribution of responses to dopaminergic drugs, with 12/16 PD subjects demonstrating increased AVA of the slower-swinging arm and reduced ASA with dopaminergic treatment. Overall, ASA was significantly reduced with dopaminergic treatment ($p=0.0386$), whereas MXC was unchanged ($p=0.7436$). Of note, one PD subject had particularly low MXC values in the ON-drug state. Even after removal of this subjects from the MXC analysis, the MXC remained unchanged between OFF- and ON-drug states ($p=0.5245$). AVA was significantly increased for the slower-swinging arm ($p=0.0182$) but unchanged for the fast-swing arm following dopaminergic treatment ($p=0.2312$).

ASA was correlated significantly with AVA of the slower-swinging arm ($R=-0.73824$, $p=0.0011$) but not AVA of the faster-swinging arm ($R=-0.31765$, $p=0.2306$). ASA and MXC had a trend of negative correlation with each other that did not reach statistical significance ($R=-0.48235$, $p=0.0585$).

3.3. Clinical correlations of arm swing measurements

In the OFF-drug state, there were no significant correlations between any of the arm swing measurements and duration of illness, age, UPDRS-III total motor scores, or tremor scores. The rigidity score showed a trend association with ASA ($R=-0.47942$, $p=0.0828$) and MXC ($R=0.50353$, $p=0.0664$), but none reached statistical significance.

HY scores are defined subjectively by clinical assessment of the laterality of symptoms of PD patients. As expected, ASA displayed a significant positive correlation with HY scores ($R=0.65311$, $p=0.0113$) in the OFF-drug state. Higher HY scores in the OFF-drug state also

had a trend association with AVA of the slower-swinging arm ($R=-0.50621$, $p=0.0542$).

AVA of the slower-swinging arm also displayed a trend correlation with LEDD ($R=-0.48485$, $p=0.0670$). There were no statistically significant correlations between LEDD and

ASA or MXC ($p>0.3000$). Of the 4 subjects who showed no improvement from OFF- to ON-drug states, 3 represented the lowest 3 LEDD values (250 mg, 250 mg, and 300 mg) among the PD sample. Comparison of LEDD values revealed that the 4 non-responding PD subjects had significantly lower LEDD values compared to the 12 subjects whose ASA improved following drug administration ($p=0.0418$).

For PD subjects, we also evaluated agreement between most affected side and slower swinging arm. There was no strong level of agreement between the slower swinging arm and most affected side in both the OFF-drug (62.50%, $\kappa = 0.250$) and ON-drug (65.63, $\kappa = 0.313$) state.

4. Discussion

Our data agree with prior findings that PD subjects exhibit reduced symmetry and impaired coordination of arm swing during ambulation [9–12]. Most interestingly, the current study showed that whereas arm swing velocity and symmetry may improve following acute dopaminergic treatment, bilateral coordination deficits persist. Triaxial angular velocity of arm swing can be estimated easily using portable inertial devices, and provides a quantitative measurement for capturing important dynamical features of PD-related gait dysfunction. Our results suggest that these simple and objective measurements of upper limb gait may capture aspects of both dopaminergic and non-dopaminergic pathology in PD. Further studies are warranted to investigate the longitudinal trajectory of these measurements throughout PD progression.

4.1. Dopaminergic modulation of walking arm swing in PD

Measuring range-of-motion, Crenna et al. [16] reported that arm swing amplitude improved following acute dopaminergic treatment. In the current study, we used angular velocity amplitude to gauge range of motion and arm swing asymmetry to calibrate arm swing. Consistent with Crenna et al. [16], we found that acute dopaminergic therapy increased the swing amplitude of the most affected arm, but interestingly, the swing amplitude of the faster-swinging arm did not change significantly following dopaminergic treatment, even though it is known that there is some dopamine terminal loss in the least-affected hemisphere [28]. It is possible that the lack of dopaminergic modulation of the faster-swinging arm represents a physiological ceiling of dopamine in the basal ganglia. An alternative explanation, however, is that PD subjects may exaggerate the swing of the less affected arm in a compensatory fashion to enable forward motion. We also offer the first demonstration that acute dopaminergic treatment improves arm swing symmetry, consistent with a role for dopaminergic and BG systems in PD-related arm swing deficits [29–31]. Arm swing symmetry improved in most PD subjects following drugs administration and, interestingly, the LEDD amount was significantly lower among PD subjects whose symmetry did not improve. Like Crenna et al. [16], we found that arm swing amplitude was not restored to control levels. However, we did not observe improved coordination after

dopaminergic treatment as reported by Crenna et al. [16]. Crenna et al. [16] utilized phase shift between ipsilateral arm and thigh angles to quantify inter-limb coordination, whereas the current study utilized cross-correlation to determine the extent of inter-limb statistical dependency. Thus, these differential findings regarding the effect of dopaminergic therapy on inter-limb coordination may be due to the use of different metrics.

4.2. Neural basis of human locomotion and PD-related dysfunction

Previously, upper limb gait automaticity has been thought to involve pontine nuclei, descending reticulospinal neurons, and spinal interneuronal circuits [32–34]. Recently, the pedunculopontine nucleus (PPN) has gained particular attention for its potential role in freezing of gait and falls in PD [35]. The PPN receives substantial inhibitory afferents from the globus pallidus internus and substantia nigra pars reticulata (SNr) of the BG [36, 37]. In PD, the activity of these latter BG output structures is known to be increased [38], and this excessive inhibitory drive might contribute to gait dysfunction in PD by suppressing PPN gait-related activity. Consistent with this notion, injection of bicuculline into the PPN has been shown to abolish SNr-mediated inhibition of locomotion [39]. Similarly, high-frequency stimulation of the STN has been shown to reduce SNr and GPi activity, and this may explain the observation that bilateral subthalamic stimulation improves upper limb range of motion in PD [16, 40, 41]. These lines of evidence, taken together with our finding that dopaminergic medication improves arm swing symmetry, suggest that some upper limb gait features in PD may be related to BG excessive inhibition of mesopontine locomotion centers. However, we found no improvement in arm swing coordination (specifically MXC) during the ON-drug state, suggesting that non-dopaminergic pathways also may play some role in PD-related gait dysfunction. Therefore, it is possible that MXC may provide a measure of non-dopaminergic dysfunction in PD. Consistent with the notion that some PD-related gait deficits arise from non-dopaminergic substrates, Lord et al. [6] recently demonstrated that double limb support time variability is remarkably less responsive to dopaminergic treatment than stride time variability. Moreover, MXC may be related biologically to other gait coordination deficits in PD (i.e. freezing of gait). Indeed, several studies have shown that various activities involving cyclical movements of the upper extremities can provoke motor blocks in PD patients [42–44]. It is thought that freezing episodes may represent saturation of normal compensatory mechanisms. In support of this notion, upper limb motor blocks have been associated with reduced activity of the putamen and pallidum, and with increased activation of cortical motor areas [45]. Whereas the current study could not directly address the relationship between reduced arm swing and freezing of gait, there may be some overlap in the neural basis for these clinical manifestations.

In addition to investigating the central mechanisms of gait dysfunction, previous experiments also have attempted to shed light on the neuromuscular processes that may give rise to impaired upper-limb gait function in PD. Buchthal and Fernandez-Ballesteros [13] demonstrated that reduced arm range of motion during walking may be related to mistimed activation of the deltoid muscles in PD subjects. They reported that reduced arm swing was not sufficiently explained by rigidity alone. In agreement with this hypothesis, we found that none of the arm swing measurements were correlated with rigidity scores. The lack of correlation in the present study, however, maybe due to a small sample size and varying

disease severities. In addition, the maximal cross-correlation between arms was not modulated by dopaminergic treatments. Lastly, the side of the slower-swinging arm did not have strong correspondence with the most affected side in PD subjects, although this lack of correspondence may be attributable to the circular nature of the track. Together, these results underscore the need to investigate further the role of both dopaminergic and non-dopaminergic mechanisms responsible for PD-related gait dysfunction.

4.3. Limitations

The current study had several limitations. First, the dosage and type of dopaminergic therapy was patient-dependent and was not consistent across PD subjects. In addition, a number of dopaminergic drugs (i.e. MAO-B inhibitors and dopamine agonists) have very long half-lives, and moreover, the dopamine produced from levodopa activates both D₁ and D₂ receptors, whereas the dopamine agonists are essentially D₂ selective, further complicating how to define the OFF-state. Although our OFF procedure is standard practice in the field [46], these pharmacologic factors may have contributed to considerable variation in the arm swing measurements following dopaminergic therapy. Nonetheless, we found significant modulation of arm swing following dopaminergic drug administration in our study. Second, because we sought not to make any of the subjects uncomfortable during testing, the distances walked were quite variable although contingency analysis suggested that trial distances were not systematically biased between or within groups (Table 1). Third, gait speeds could not be calculated precisely using different trial lengths and portable sensors, and they may play an independent role in arm swing amplitude. It is notable, however, that the AVA of the faster-swinging arm was unaffected by dopaminergic drugs, whereas the AVA of the slower-swinging arm improved. These differential effects on the slower- and faster-swinging arms suggest a role for dopaminergic modulation of impaired arm swing. Fourth, the amount of trunk torsion during gait could not be recorded using portable wrist sensors and may have contributed to reduced arm swing amplitude in one or both arms among PD subjects. Lastly, the current study was limited by its cross-sectional nature, lack of drug-naïve PD subjects and involving PD subjects in different stages and duration of illness, and the inability to track gait symptoms longitudinally. Future studies may benefit from studying the effects of dopaminergic drugs of specific types among these subjects and, accordingly, how gait changes as a function of acute and chronic therapy.

4.4. Conclusions

In summary, the present study confirms previous findings of upper-limb gait dysfunction in PD, and provides additional insight into the relationship between dopaminergic replacement and arm swing. Our findings that acute dopaminergic therapy improves arm swing velocity and symmetry are consistent with known asymmetric nigrostriatal dopamine depletion in PD. Bilateral coordination was, however, not improved by dopaminergic treatment and no correlations were observed between arm swing measurements and rigidity scores. Taken together, these findings suggest that dopamine and non-dopaminergic systems may play distinct roles in PD-related upper-limb gait deficits, the relative role of which deserves further investigation. Further studies are warranted to characterize the longitudinal trajectory of arm swing dynamics throughout PD progression.

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Abbreviations

ASA	Arm swing asymmetry
AVA	angular velocity amplitude
FSA	faster-swing arm
LEDD	levodopa-equivalent daily dose
MXC	maximum cross correlation
PD	Parkinson's disease
SSA	slower-swinging arm
UPDRS-III	Unified Parkinson's Disease Rating Scale part III

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Figure 1.

Triaxial angular velocities (radians/second) recorded from the right arm during a single trial from a control subject (left) and a single trial from a PD (OFF-medication) subject (right). Original unfiltered measurements are depicted in the top row and low-pass filtered (<2Hz) data are depicted in the bottom row. Unfiltered sensor data from the PD subject are notable for tremor artifacts (top right), which are mitigated using the low pass filter (bottom right). Bidirectional arrow vectors represent the trajectory of the largest principal component of the right arm, computed from aggregate control data.

Figure 2.

Arm swing measurements among PD and control subjects. Center horizontal bars represent medians, pluses denote means, upper and lower hinges represent first and third quartiles, and vertical lines extend to observations that are within 1.5 IQR of the upper or lower hinges.

Abbreviations: Arm swing asymmetry (ASA), maximum cross correlation MXC, and angular velocity amplitude (AVA) of the faster-swing arm (FSA) and slower-swinging arm (SSA).

Table 1

Demographic, clinical, and walking trial information of all subjects

	Controls	PD subjects	
Number of subjects	17	16	
Gender (F : M)	6 : 11	8 : 8	
Age (SD) (years)	61.82 (8.70)	64.27 (6.92)	
Dominant hand (Right : Left)	12 : 5	16 : 0	
Duration of illness (SD) (years)	N/A	2.47 (3.01)	
Hoehn & Yahr (SD) Stage	N/A	1.81 (0.65)	
LEDD (SD) (milligram)	N/A	520.88 (239.39)	
Most Affected Side (Right : Left)	N/A	7 : 9	
Medication status	N/A	<i>“OFF”</i>	<i>“ON”</i>
UPDRS-III scores (SD)	4.2 (4.6)	20.0 (7.1)	14.0 (5.7)
Number of subjects who			
Completed 0.5 miles (2 laps)	6	7	6
Completed 0.25 miles (1 lap)	11	6	6
Completed 0.17 miles (2/3 lap)	0	3	4

Abbreviations – LEDD: Levodopa equivalent daily dose; UPDRS: Unified Parkinson's disease Rating Scale;

Table 2

Clinical and arm swing measurements for all subjects. The data presented are the mean and standard deviation (in parentheses).

Parameter	Control subjects	PD subjects		P-Value	
		Off-Drug	On-Drug		Off vs. Control
United Parkinson's Disease Rating Scale – Part III – motor scores					
<i>Total</i>	N/A	20.0 (7.05)	14.0 (5.72)	<0.0001	0.0016
<i>Tremor</i>	N/A	0.294 (0.257)	0.225 (0.275)	0.0004	0.2930
<i>Rigidity</i>	N/A	1.83 (2.00)	1.11 (1.22)	0.0002	0.0015
Arm swing measurements					
<i>ASA</i>	20.47 (16.79)	46.56 (25.23)	39.38 (25.42)	0.0046	0.0386
<i>MXC</i>	0.9275 (0.081)	0.7865 (0.1959)	0.8232 (0.1928)	0.0026	0.7436
<i>AVA_{FSA}</i>	2.313 (0.731)	2.007 (0.771)	2.173 (0.696)	0.2801	0.2312
<i>AVA_{SSA}</i>	1.710 (0.684)	0.867 (0.480)	1.159 (0.729)	0.0018	0.0182
<i>SSA (Right : Left)</i>	0 : 17	3 : 13	2 : 14	N/A	N/A
<i>FSA (Right : Left)</i>	17 : 0	13 : 3	14 : 2	N/A	N/A

Abbreviations - AVAFSA angular velocity amplitude of the faster-swinging arm; AVASSA angular velocity amplitude of the slower-swinging arm; ASA: arm swing asymmetry; MXC: maximum cross-correlation between arms; UPDRS: Unified Parkinson's disease Rating Scale;