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# Variability of anticipatory postural adjustments during gait initiation in individuals with Parkinson's disease

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#### Abstract

**Background and Purpose**—In people with Parkinson's disease (PD), difficulties with initiating stepping may be related to impairments of anticipatory postural adjustments (APA). Increased variability in step length and step time has been observed in gait initiation in PD. In this study, we investigated whether the ability to generate consistent APAs during gait initiation is compromised in individuals with PD.

**Methods**—Fifteen individuals with PD and eight healthy control subjects were instructed to take rapid forward steps following a verbal cue. The changes in vertical force and ankle marker position were recorded via force platforms and a three-dimensional motion capture system respectively. Means, standard deviations, and coefficients of variation of both timing and magnitude of vertical force as well as stepping variables were calculated.

**Results**—The time interval was longer and force modulation was smaller during the postural phase of gait initiation in individuals with PD. Both the variability of timing and force modulation was larger in individuals with PD. Individuals with PD also had a longer time to complete the first step but no significant difference was found for the variability of step time, length, and speed between groups.

**Discussion and Conclusion**—The increased variability of anticipatory postural adjustments during gait initiation could affect the posture-locomotion coupling, and lead to start hesitation, and even falls in individuals with PD. Future studies are needed to investigate the effect of rehabilitation interventions on the variability of anticipatory postural adjustments during gait initiation in individuals with PD. Video Abstract available for more insights from the authors (see Supplemental Digital Content 1)

#### Introduction

Disorders of posture and gait are the most debilitating symptoms in individuals with Parkinson's disease (PD) as they often restrict functional independence and are a major cause of morbidity and mortality. Gait initiation requires a transition from static posture to dynamic locomotion, and the difficulty with initiating gait is a common problem for

individuals with PD especially those at advanced stage.<sup>1,2</sup> For forward stepping, anticipatory postural adjustments (APAs) normally involve a sequence of muscle activations and corresponding changes in the ground reaction forces that move the net center of pressure (CoP) beneath the feet backward and toward the initial swing limb.<sup>3</sup>—<sup>5</sup> This actively generated motor sequence produces the forces and moments necessary to propel the body center of mass (CoM) forward and towards the single stance limb prior to stepping. Thus, these neuromechanical elements represent the control parameters for posture and locomotion during the initiation of gait.

Changes in both kinematic and kinetic parameters during gait initiation have been reported in individuals with PD.<sup>6</sup>\_16 Compared to healthy subjects, the ground reaction forces characterizing APAs are prolonged in duration and reduced in amplitude in both mediolateral and anteroposterior directions, resulting in the longer delays between the APA and step onset.<sup>6</sup>\_8,10,12 Individuals with PD also display impaired stepping performance with shorter stride length and slower step speed.<sup>14</sup>,15 These findings indicate that the impairments of gait initiation may result from the bradykinetic and hypokinetic APAs reflecting timing and amplitude scaling difficulties in PD.<sup>13</sup> In addition, Jacobs et al<sup>17</sup> observed that the freezing of gait induced by backward translation of the supporting surface is usually accompanied by multiple APAs with no delay in onset and similar amplitude as single APAs observed in controls, suggesting that the gait initiation difficulties could also be caused by a disruption in the normal posture-locomotion coupling of the stepping in individuals with PD. Other impairments in the normal spatiotemporal coupling between posture and locomotion have been identified in other studies of gait initiation among people with PD.<sup>12,14,16,18</sup>

Variability of gait is an indicator of the ability to produce a steady gait rhythm. 19,20 Increased variability of gait and freezing of gait have been considered as manifestations of arrhythmicity and disturbances in the dopamine-mediated locomotor network for steady state walking. <sup>21,22</sup> Compared to healthy older adults, variability of step length also has been found to be greater in PD during gait initiation with self-selected and maximal speed.<sup>8,15</sup> The neural circuits involved in the APA generation are thought to include the supplementary motor area (SMA) and are independent from the volitional lifting of the foot during gait initiation.<sup>23</sup> Cortical activity in preparation for perturbation also appears to be independent of postural response strategy. The observation of multiple APAs associated with freezing of gait during gait initiation and the enhancement of APA parameters with external sensory and mechanical stimuli may imply that the force modulation during preparation phase of gait initiation could be more variable in PD. 12,14,16,17 The increased variability of APA could hamper the ability of force production to alter the CoM-CoP relationship required for gait initiation, leading to the abnormal coupling between posture and locomotion component of the stepping, and resulting in start hesitation in individuals with PD. Furthermore, previous findings of APA impairments with no change in stepping performance during gait initiation in PD also suggest that the APA impairments (i.e. increased variability in force modulation) may serve as an early marker for later developing problems (i.e. increased variability of step length).24

Despite the functional significance of APAs to stepping performance during gait initiation, it remains unclear whether an increased variability observed in stepping performance may also

be presented in APA in PD. This issue has important implications for rehabilitation interventions and fall prevention. Therefore, the purpose of the present study is to determine whether the variability of APA parameters during gait initiation is modified in individuals with PD compared with healthy controls. We hypothesized that individuals with PD would demonstrate greater variability in APA kinetic parameters (vertical ground reaction force timing and magnitude) and stepping variables (step length, step time, and step speed) of gait initiation.

#### **Methods**

#### **Participants**

Fifteen individuals with moderate PD and eight healthy control subjects participated in the study. Individuals with PD were recruited from the Parkinson's Disease and Movement Disorders Center at Northwestern University and Maryland Parkinson's Disease and Movement Disorders Center. Inclusion criteria for PD included: 1) a diagnosis of adult idiopathic onset; 2) stage 2-3 of the Hoehn and Yahr disability scale; <sup>25</sup> 3) a history of FOG supported by self-report using UPDRS-II;<sup>26</sup> 4) a stable regimen of medication; 5) ability to walk at least 10 m without assistance; 6) dyskinesias < 3 on the United Parkinson's Disease Rating Scale (UPDRS);<sup>26</sup> 7) no history of brain surgery or placement of a deep brain stimulator; 8) a score > 24 on the Mini Mental State Examination.<sup>27</sup> The exclusion criteria for both groups included: 1) evidence of any clinical significant functional impairments including cardiovascular, pulmonary, metabolic, musculoskeletal, or neurological disorders; 2) any uncorrected vision or hearing problems that limit daily activities or communication. PD subjects were assessed during the peak dose of their medication. Participant characteristics are indicated in Table 1. Before participating in the study, all participants signed a written informed consent approved by the Institutional Review Board at Northwestern University School of Medicine and University of Maryland School of Medicine.

#### **Experimental setup and protocol**

Participants began each trial standing stationary on an elevated walkway set 38.1 cm above the ground. The feet were positioned comfortably and as parallel as possible over two separate force platforms. The foot placement was kept consistent by marking the position of the feet on the contact surface. Subjects wore a safety harness attached by straps to a low friction trolley system on an overhead track to prevent falls without otherwise interfering with movement. During the testing, participants self-initiated a series of three steps forward as fast as possible at a self-selected time following a "get ready" cue. Subjects initiated the step with their preferred leg, and trials in which they leaned or stepped with non-preferred limb were discarded. Participants were asked to declare their preferred limb for kicking a ball. Discarded trials were repeated whenever possible.

### Data collection and analysis

Vertical ground reaction forces were recorded using two strain-gauge force platforms (AMTI, Newton, MA) with sampling frequency at 500 Hz. Three dimensional kinematic data was collected using a 6-camera motion capture system (Vicon, Lakeforest, CA) at 120

Hz. Reflective markers were attached on subject's left and right lateral malleoli and were used to determine the stepping performance. Both kinetic and kinematic data were filtered at 40 Hz using a 2<sup>nd</sup> order low-pass Butterworth filter.

APAs were assessed by the changes of the vertical ground reaction forces (Fig. 1). APA onset of the stepping limb occurred when the vertical forces went above three standard deviations from the baseline values. APA onset of the stance limb occurred when the vertical force fell below three standard deviations from the baseline. The time instants when the vertical force of stepping and stance limbs reached the maximum value (Fz(max)), and when the vertical force of stance limb reached the minimum value (Fz(min)) were identified. The time when the vertical force of the stepping and stance limbs reached the zero value (Fz(zero)), signifying foot-off from the force platform, was also identified. The time intervals from APA onset to these points were also calculated. The magnitude changes of the vertical force from the APA onset to the maximum value of the stepping limb, and from the APA onset to the minimum and maximum value of the stance limb were determined and normalized to each subject's body weight.

The beginning and ending of the step was defined as the moment when the vertical velocity of reflective marker on subjects' malleoli went above and fell below three standard deviations from its baseline respectively (Fig. 1). Three stepping performance variables were calculated including 1) step duration: time difference between the beginning and ending of the first step; 2) step length: the horizontal distance traveled by the marker during the first step; 3) step speed: step length divided by step time.

#### Statistical analyses

Means and standard deviations (SD) were calculated for each subject across five trials for all variables. The coefficient of variation (CV = SD/Mean \* 100%) was calculated to represent within-subject variability for all variables. Because of the relatively small sample size, nonparametric Mann-Whitney U tests were performed to assess the differences in both mean and variability values between the two groups. All statistical analyses were carried out with version 22 of the SPSS statistical software (SPSS Inc., Chicago, IL). The significance level was set at p 0.05.

#### Results

#### APAs: timing

The CV of the time intervals from stepping-foot APA onset to Fz(max) and Fz(zero) were significantly larger (by 169% and 125% respectively) in PD than HC (U=7, p<0.01, r=0.71, and U=15, p<0.01, r=0.61) (Fig 2a). The CV of the time intervals from stance-limb APA onset to Fz (min) and Fz (zero) were also significantly larger (by 157% and 130% respectively) in PD compared to HC (U=15, p<0.01, r=0.61, and U=18, p<0.01, r=0.57) (Fig 2a). The CV of the time interval of stance-limb APA onset to Fz(max) also approached significance (U=31, p=0.06, r=0.39) (Fig 2a). Longer time intervals of stepping-limb APA onset to Fz(zero) (U=13, p<0.01, r=0.63), and stance-limb APA onset to both Fz(max) and

Fz(zero) (U=17, p<0.01, r=0.58, and U=4, p<0.01, r=0.75) were observed in PD compared to HC (by 36%, 47%, and 35% respectively) (Fig 2b).

#### **APAs: force modulation**

For the stepping limb, the CV of the vertical force modulation from APA onset to Fz(max) was significantly larger (by 104%) in PD than HC (U=19, p<0.01, r=0.55) (Fig 3a). For the stance limb, the CV of the vertical force modulation from APA onset to Fz(min) was significantly larger (by 100 %) in PD than HC (U=19, p<0.01, r=0.55) (Fig 3a). No significant difference between groups was found for the CV of the vertical force modulation of the stance limb from APA onset to Fz(max).

For the stepping limb, the increase of the vertical force from APA onset to Fz(max) was significantly smaller (by 59%) in PD compared to HC (U=3, p<0.01, r=0.77) (Fig 3b). For the stance limb, the changes of the vertical force from APA onset to Fz(min) and Fz(max) are also significantly smaller (by 58%) in PD than HC (U=10, p<0.01, r=0.67 and U=26, p=0.03, r=0.46) (Fig 3b).

#### Stepping performance

CV and means of first step time, step length, and step speed during gait initiation in PD and HC are presented in Table 2. No significant differences in the CV of step time, step length, and step speed were found between two groups. Individuals with PD took a longer time (by 54 %) to complete a step than healthy controls (U=5, p<0.01, r=0.74). There was no significant difference in stride length between the groups (U=60, p=1.0). As a result, the step speed was slower in PD compared to HC (U=15, p<0.01, r=0.61).

#### **Discussions**

The objective of the present study was to investigate the variability of timing and magnitude of the vertical ground reaction forces during APAs of gait initiation in PD. Overall, we have shown that individuals with PD displayed greater variability in both timing and magnitude of the vertical ground reaction force during APAs of gait initiation compared to healthy adults.

Consistent with previous studies, individuals with PD in the present study had a slower speed in executing the first step, confirming the temporal impairments of gait initiation. <sup>14,15</sup> Despite no statistical significance in the variability of the stepping performance variables between the groups, the difference in step time variability between groups is slightly larger in the present study compared to a previous study by Roemmich et al. involving a larger sample of PD participants (see Table 2, and CV of step length=10±0.76 for PD and 7.4±0.54 for HC in Roemmich et al.). <sup>15</sup> Hence, the lack of statistical significance between groups may be due to the relatively smaller sample size which might have limited statistical power in the present study.

In addition to the stepping performance variables during gait initiation, APAs are necessary for mediolateral balance stability and for unloading the swing leg and thus creating the conditions for forward stepping. <sup>12,14,16</sup> Bradykinesia and hypokinesia are the cardinal symptoms in PD, and defined as decreased amplitude and speed of movement,

respectively.<sup>28</sup> Consistent with previous studies, our findings of the longer duration and smaller magnitude of force modulation during APA of gait initiation suggest that bradykinesia and hypokinesia would affect not only movement execution but also movement preparation involving postural elements in PD at moderate stage.<sup>8</sup>–<sup>10,12,14</sup>

Our novel observations on APA variability extend those from prior work by showing that the timing and magnitude of the vertical force modulation is more variable in PD than in healthy controls. The significant APA variability but not variability in stepping performance between groups, is consistent with the model proposed by Massion<sup>23</sup> with separate, interacting motor programs for neural control of APAs and the step itself. The neural circuits responsible for the control of APAs are thought to include the SMA of cortex and basal ganglia, and are organized subcortically with the pontomedullary reticular formation involved in the control of posture through brain stem-spinal pathways. <sup>29</sup>\_31 The motor cortical command for a goal-intended movement generated by a neural circuit including the dorsolateral premotor cortex and primary motor cortex might include feedforward signals for generating the postural adjustments that anticipate and accompany movements. <sup>29</sup>—<sup>31</sup> As a result, the timing of the postural responses is thought to be linked to the cortical command for the voluntary initiation of movement. In this manner, it is possible that the increased variability of force modulation during the postural preparation phase of gait initiation may have resulted from increased cortical control due to the deficits in neural control involving the SMA and basal ganglia in PD.<sup>23,30</sup> Furthermore, the findings of increased variability in neuromechanical force modulation during the preparation phase but not while stepping also suggested that the identification of APA impairments at an earlier stage of PD, may be helpful to developing rehabilitation interventions directed at minimizing or slowing the progression of further stepping abnormalities during gait initiation. <sup>18</sup>

Studies of gait initiation in healthy subjects have shown that interlimb spatio-temporal coordination between legs is necessary for shifting the center of pressure laterally toward the initial swing leg in order to propel the CoM toward the initial stance leg. <sup>3,4,32</sup> However, Parkinson's disease is typically an asymmetrical disease because the motor symptoms usually affect one side of the body first, and the initially affected side remains most prominently affected with the contralateral side involved later in 80 percent of PD patients. <sup>33,34</sup> Thus, such motor asymmetry could differentially affect the sides of the body with respect to balance control in standing and gait in PD. <sup>35</sup>–<sup>37</sup> The time to unload the initial swing leg normally corresponds with the timing of maximum limb loading on the initial stance leg during gait initiation. Our findings of the timing variability from APA onset to zero vertical force at limb lit-off on the initial swing leg and the time of maximum vertical force on the initial stance leg showed a significant group difference in the former variable but not the latter. This interlimb difference temporal variability suggested that motor asymmetry could also affect the interlimb coordination of force modulation during gait initiation in PD.

A conceptual modal has been proposed for developing therapeutic interventions that target APA-locomotion coupling impairments during gait initiation in PD.<sup>18</sup> In this scheme, a step will be initiated when sufficient anticipated postural state conditions for balance stability related to the relationship between the CoM and BOS are achieved by APAs generating the

weight transfer from bipedal to single limb support.<sup>18</sup> Using this framework, both acute and immediate improvements in gait initiation have been observed with the application of external mechanical or sensory stimuli applied early in the postural adjustment phase that assists the APAs by facilitating weight transfer and achieving a more stable anticipated postural condition prior to the initiation release of stepping.<sup>12,14,16</sup> It remains to be determined, however, whether the variability of APA parameters during gait initiation may also be improved through external postural enhancement to modify posture-locomotion coupling with practice training.

Among the limitations of the present study were the small sample size that may have contributed to our finding of some non-significant differences between groups. We also focused only on participants with moderate to severe stage PD, so that the findings may not be generalizable to individuals with less advanced stages of PD. Moreover, the participants with PD were only tested in the medications "on" state. Stride time variability has been found to be deceased in PD patients in the "on" state compared to the "off" stage, suggesting a positive effect of levodopa on gait variability.<sup>38</sup> Hence, the comparison of the variability of APA during gait initiation in the medications "on" and "off" conditions for the same group of subjects would provide further understanding on the extent to which the variability of APAs during gait initiation is affected by the dopaminergic system.

#### **Conclusions**

In summary, the bradykinetic and hypometric APAs, and the abnormal spatial and temporal coordination between APA and stepping components of gait initiation may lead to start hesitation, subsequent freezing of gait, and possibly an increased risk of falls in PD. The present study has shown increased variability of timing and magnitude of vertical loading and unloading forces with longer duration and smaller vertical force during gait initiation in individuals with PD compared to healthy control subjects. Future studies are warranted to determine the relationship between the variability of APAs during start hesitation of gait initiation and freezing episodes as well as in relation to the risk of falls in PD. Based on the previous findings of an association between the variability of gait and both freezing and risk of falls, additional information is needed to determine whether improving the variability of APAs and stepping performance variables might help to alleviate such motor impairments in PD.

# **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

# Acknowledgments

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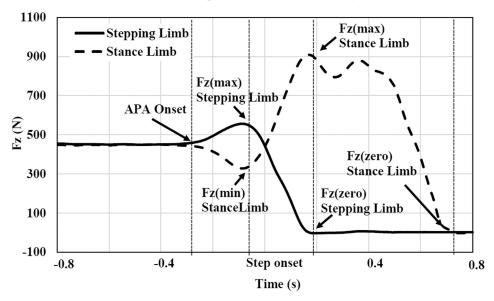
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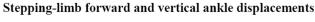
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A

### Vertical ground reaction forces (Fz)



В



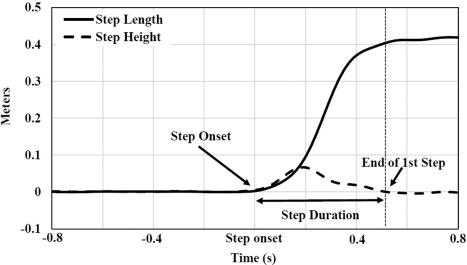
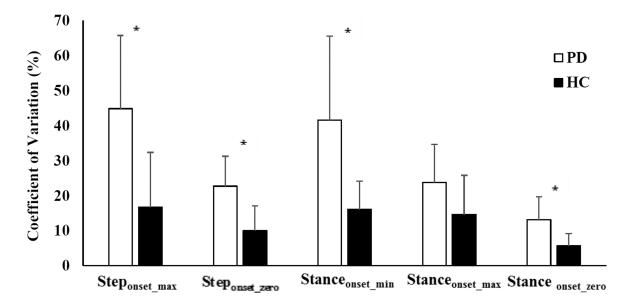


Figure 1.

Time series of vertical ground reaction forces in the vertical direction (Fz) (A) and ankle marker displacement (B) from the onset of the anticipatory postural adjustments (APAs) to the landing of the stepping limb.

 $\mathbf{A}$ 



В

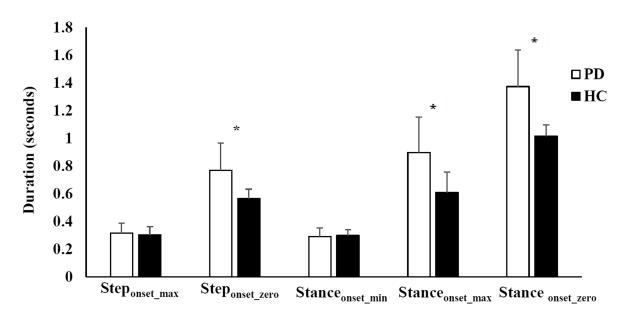
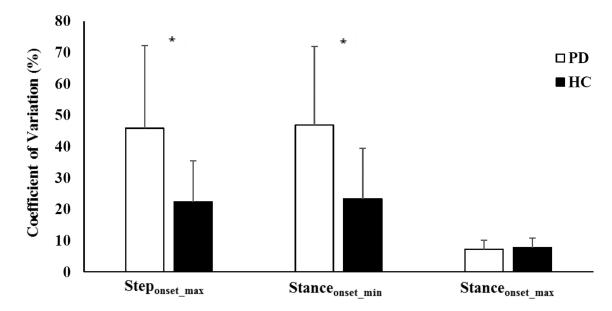


Figure 2. Coefficients of Variation (A) and Group Means (B) of time intervals for anticipatory postural adjustment (APA) onset to maximum vertical ground reaction force of stepping limb, APA onset to minimum and maximum vertical ground reaction force of stance limb in individuals with Parkinson's disease (PD) and healthy control subjects (HC). Error bars are standard errors of the mean. \*P < 0.05.

A



B

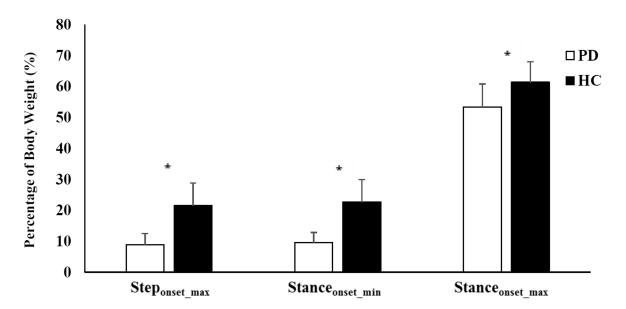


Figure 3. Coefficients of Variation (A) and Group Means (B) of anticipatory postural adjustment (APA) magnitudes for APA onset to maximum vertical ground reaction force of stepping limb, and APA onset to minimum and maximum vertical ground reaction force of stance limb in individuals with Parkinson's disease (PD) and healthy control subjects (HC). Error bars are standard errors of the mean. \*P < 0.05.

Table 1

Characteristics of the individuals with Parkinson's disease (PD) and healthy control subjects (HC)

Hoehn & Yahr	2.5±0.4 (2-3)	NA
Hoehn		_
PD duration (years)	8.1±6.1 (1-23)	NA
Gender (Male/Female)	11/4	5/3
Age (years)	73.1±8.5	73.3±9.1
Number	15	8
	PD	НС

Values presented in the table are mean  $\pm$  standard deviation, unless otherwise noted.

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Table 2

Group Means and coefficients of variation (CV) for step time, step length, and step speed during gait initiation in individuals with PD and healthy control subjects (HC).

	Step Time (s)	ime (s)	Step Length (m)	ngth (m)	Step Speed (m/s)	ed (m/s)
	Mean	CV (%)	Mean	CV (%)	Mean	CV (%)
PD	0.80±0.05*	12.28±1.56	$0.53\pm0.03$	7.63±1.15	$0.80 \pm 0.05^{*}  12.28 \pm 1.56  0.53 \pm 0.03  7.63 \pm 1.15  0.71 \pm 0.06^{*}  12.44 \pm 1.73$	12.44±1.73
НС	HC 0.52±0.02	$8.82\pm1.46$	$0.53\pm0.02$	$9.30\pm1.50$	$8.82{\pm}1.46 \qquad 0.53{\pm}0.02 \qquad 9.30{\pm}1.50 \qquad 1.03{\pm}0.06 \qquad 13.35{\pm}2.14$	$13.35\pm2.14$
	20:0-1	0.02	20:0-0:0		3	00:0-0:1

Values presented in the table are mean  $\pm$  standard error.

 $_{\star}^{*}$  indicates significant difference between groups,  $p < 0.05. \label{eq:control_fit}$