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Step initiation in Parkinson's disease: Influence of initial stance conditions

Laura Rocchi [a,*], Lorenzo Chiari [a], Martina Mancini [a], Patricia Carlson-Kuhta [b], Anne Gross [b], Fay B. Horak [b]

[a] *Biomedical Engineering Unit, Department of Electronics, Computer Science & Systems, University of Bologna, Viale Risorgimento 2, 40136 Bologna, Italy*
[b] *Neurological Sciences Institute, Oregon Health & Science University, 505 NW 185th Avenue, Beaverton, OR 97006, United States*

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Abstract

In this study, we investigated how the size of preparatory postural adjustments prior to step initiation, and step length and velocity depend on initial stance width in patients with Parkinson's disease (PD) both in the ON and OFF levodopa states and in healthy elderly subjects. Twenty-one subjects with idiopathic PD and 24 age-matched healthy control subjects took two steps starting with feet on a two-plate force-platform, from either narrow or wide stance width. We measured how the magnitude of anticipatory postural adjustments (APA) and step characteristics scaled with stance width. Results showed that preparation for step initiation from wide stance was associated with a larger lateral and backward center of pressure (CoP) displacement than from narrow stance. Velocity and length of the first step were also sensitive to initial stance conditions, probably in relation with the differences in the corresponding APA. On the contrary, the duration of APA was not significantly affected by initial stance width, but it was longer in PD compared to healthy subjects, and speeded up by levodopa. Although subjects with PD did scale up the size of their APA with stance width, they had much more difficulty initiating a step from a wide stance than from a narrow stance, as shown by the greater differences from control subjects in the magnitude of the APA. Our results support the hypothesis that PD subjects maintain a narrow stance as a compensation for their inability to sufficiently increase the size of their lateral APA to allow fast step initiation in wide stance.

Keywords: Parkinson's disease; Step initiation; Adaptation; Scaling; Basal ganglia

Step initiation is a complex motor task that entails the transition from a quiet standing posture in double-limb support, to dynamic equilibrium that allows forward body progression. Step initiation involves a preparatory phase and a stepping phase, both of which are thought to be controlled by parallel pathways from secondary and primary motor cortex areas, respectively [18]. The preparatory phase involves anticipatory postural adjustments (APA) in which the center of pressure (CoP) shifts backward and toward the swing limb, to move the body center of mass (CoM) forward and over the stance limb, in preparation for single-limb support [2,6,18]. The stepping phase begins when the weight has been transferred to the stance limb and in particular the velocity of the step was found to correlate with the magnitude of APA [16,22].

Problems with step initiation, clinically identified as 'start hesitation', are common in Parkinson's disease (PD) and disturbances in the APA are considered the major pathophysiological mechanism that underlies hindered gait initiation in PD subjects [2,6]. Start hesitation in PD is associated with diminished and prolonged preparatory CoP displacements as well as reduced step length and velocity, compared to age-matched control subjects [2,6,11,24]. Both the preparatory and stepping phases of step initiation are improved by levodopa medication [2]. Previous studies suggested that the APA may be impaired in PD because of the many connections of the basal ganglia with the supplementary motor area and the premotor area of the cortex, both of which are implicated in movement preparation [18,19] or with the penduncular pontine nucleus in the brainstem, which is implicated in locomotion initiation [21]. Gait initiation problems in subjects with PD may also originate from changes in the basal ganglia that result in slowing of the sequential execution of the preparatory and stepping subcomponents of the task [24].

Like all motor programs, the motor program for step initiation needs to change when characteristics of the motor task change: e.g. the APA prior to step initiation adapts to initial asymmetric

* Corresponding author. Tel.: +39 051 209 3904; fax: +39 051 209 3073.
E-mail address: lrocchi@deis.unibo.it (L. Rocchi).

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weight loading [22], and to initial stance on a narrow beam [5]. Previous studies have shown that PD impairs adaptation of the APA prior to rising to toes [10] and of reactive postural responses when the conditions of support change [3,15,25]. However, the effects of initial stance width on adaptation of the APA and step characteristics, such as the effects of PD on this adaptation, are unknown.

Because of the importance of unloading the initial swing limb prior to a step, we supposed that the size of the preparatory postural adjustments prior to step initiation would depend on initial stance width. Since PD is associated with a narrow stance width, we hypothesize that narrow stance width may be a compensation for the inability to generate large enough APA in a wider stance.

The aims of the present study were: (1) to understand how healthy elderly and PD subjects adapt their postural preparation for a step when initial stance changes from narrow to wide and (2) to investigate the effect of levodopa on step preparation and adaptation.

Twenty-one subjects with idiopathic PD (16 males, 5 females, age 61.7 ± 7.8 years, disease duration 16.2 ± 9.2 years), and 24 age-matched healthy control subjects (18 males, 6 females, age 62.4 ± 7.4 years), free of any neurological or musculoskeletal disorders, participated in this study, after giving informed consent in accordance with OHSU Institutional Review Board regulations for human subject studies. Three of the PD subjects could not be tested in the OFF state, as their symptoms were too severe to complete the wide stance trials. There was no difference in height between the two groups (mean ± S.D., PD = 1.77 ± 0.1 m; control = 1.75 ± 0.1 m). The PD subjects were first tested in the practical OFF state, with a medication washout of at least 12 h and again on levodopa medication, at least one hour after taking their usual dosage (ON state). The Motor Section (III) of the UPDRS was administered immediately before each test condition [9]. Control subjects completed two sets of trials to match the two states of the PD subjects. The repetition allowed us to check for the possible presence of any trend of fatigue or learning effect due to the repetition of trials.

At the start of each trial, the subjects stood with each foot on separate side-by-side force plates. They were instructed to voluntarily take two steps, starting with the right foot, at their normal, comfortable pace. Three trials of step initiation were acquired, starting with feet parallel, 5 cm apart (narrow stance) and then 26 cm apart (wide stance). Initial stance position and symmetrical weight loading were made consistent from trial to trial by tracing foot outlines and by monitoring anterior–posterior and medio-lateral CoP position.

We acquired force-platform and kinematic data (Fig. 1). Four vertical forces under each force plate were used to calculate the position of the total body CoP (*i.e.*, the application point of the total ground-reaction force). The lateral CoP excursion toward the initial swing limb and the symmetrical changes of the vertical forces recorded from the two force plates were used to detect the APA [2]. The APA magnitude was measured both by the peak of the antero-posterior CoP excursion in the backward direction and by the peak of lateral CoP excursion towards the swing foot. The APA timing was measured by the foot-off latency, computed from the onset of the first measurable change in lateral

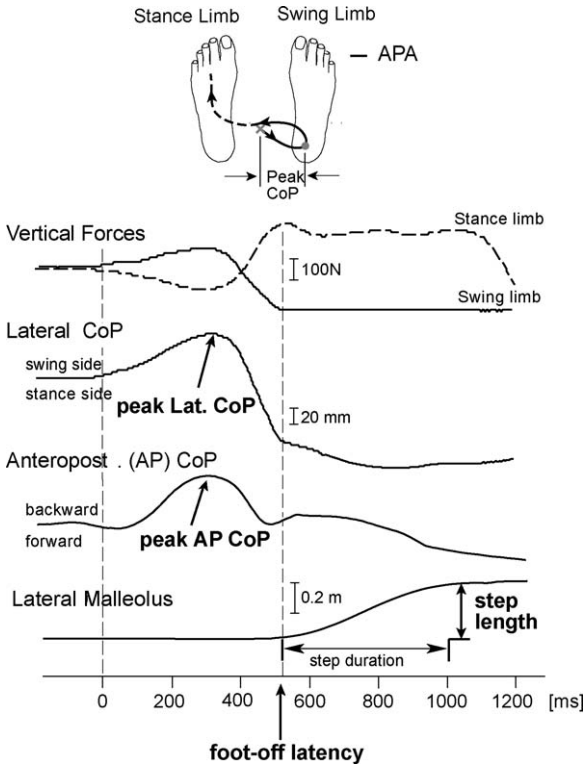

Fig. 1. Data collected in each trial and their relative timing from a representative control subject during step initiation. The schematic feet at the top show the trajectory of the CoP during the APA. The onset of the APA (first lateral displacement of the CoP) is defined as 0 ms and the variables peak CoP displacement, foot-off latency and step length, are shown in bold. Step velocity was measured as step length divided by step duration.

CoP to the time of foot-off (*i.e.*, the instant the initial swing limb left the force plate). Data from the force-platform were acquired at 480 Hz and low-pass filtered at 50 Hz. Length and velocity of the first step were measured with a reflective marker placed on the right lateral malleolus detected by infrared cameras (Motion Analysis Inc., Santa Rosa, CA, USA). Kinematic data were acquired at 60 Hz. Length and velocity of the first step were expressed as percentage of subject's height.

In Fig. 1, an example of data collected and the relative timing for a control subject are represented, together with the main dependent variables considered to characterize the preparation and execution phases.

The relation between clinical scores and adaptation of the APA to stance width was investigated by linear regression analysis between the UPDRS and the change in peak of lateral CoP from narrow to wide stance, both in ON and OFF states. The effect of levodopa was investigated by correlating the change, from OFF to ON, in the UPDRS and in the peak lateral CoP, both in narrow and wide stance.

Differences in adaptation between groups of subjects were detected with a 2-factors (stance and group) ANOVA (repeated measures). Sensitivity to stance width (adaptation) of the APA and of the step properties within group of subjects, were detected with a 1-factor (stance) ANOVA (repeated measures). All the analyses were performed using NCSS Software, Kaysville, Utah [13].

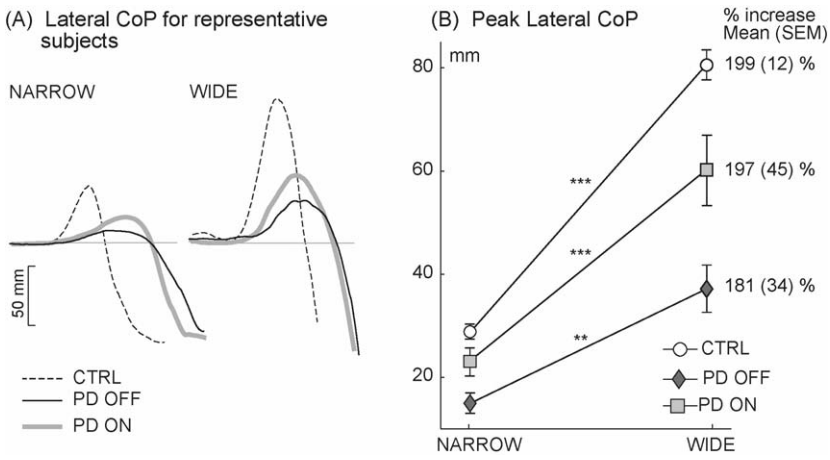

Fig. 2. Scaling of APA from narrow to wide stance. (A) Lateral CoP excursion during APA in narrow and wide stances for a representative control and PD subject, OFF and ON levodopa. (B) Mean values ± S.E.M. of peak of lateral CoP during narrow and wide stance, and corresponding percentage increase, of control and PD subjects. $^{***}p < 0.0001$; $^{**}p < 0.001$.

The PD subjects included in the study were responsive to levodopa, as shown by the improvement of UPDRS Motor Scores with levodopa (mean ± S.D.: 47 ± 13.6 in the OFF state, 22.4 ± 11.2 in the ON state). The Hoehn and Yahr scores were 3.3 ± 0.8 when OFF and 2.6 ± 0.7 when ON. No difference was found between the two test sessions in the control group, showing that no fatigue or learning effects occurred by the repetition of trials. Hence, in the figures and when listed, control data from the two test sessions were grouped together.

The APA magnitude, as measured by the peak lateral CoP toward the swing side, was sensitive to initial stance width, as shown in Fig. 2A by examples in narrow and wide stance in representative control and PD subjects. Adaptation from narrow to wide stance width involved increasing peak lateral CoP (Fig. 2B), from (mean ± S.E.M. in mm) 28.5 ± 1.1 to 80.7 ± 2.6 in control subjects ($p < 0.0001$), from 14.8 ± 1.8 to 37.2 ± 4.2 in PD OFF ($p < 0.001$), and from 23 ± 2.5 to 60.3 ± 6.2 in PD ON ($p < 0.0001$). Such values corresponded to a percentage increase of peak of lateral CoP in wide compared to narrow stance (mean ± S.E.M.) of 199 ± 12% in control subjects, 181 ± 34% in PD OFF, 197 ± 45% in PD ON. The PD subjects' peak of lateral CoP was significantly smaller than control subjects' ($p < 0.0001$ in the OFF state, $p < 0.05$ in ON state). Levodopa increased peak lateral CoP from the OFF state ($p < 0.05$), toward the normal range in narrow, but not in wide stance.

Regression analysis showed a significant correlation between the UPDRS and peak lateral CoP during the APA ($r^2 = 0.4$ in narrow, $r^2 = 0.5$ in wide stance, $p < 0.01$). In contrast, regression analyses did not reveal any correlation between the UPDRS and adaptation of lateral APA from narrow to wide stance, either in the OFF or ON state.

Preparation for step initiation was also associated with larger backward CoP displacement from wide than from narrow stance, both in control and PD subjects, as detailed in Table 1, along with statistics. When OFF, the PD subjects always exhibited a smaller backward CoP peak than did control subjects, while levodopa caused an increase in peak of backward CoP, which approached control values in narrow but not in wide stance.

Unlike APA magnitude foot-off latency was not significantly affected by stance width. The postural preparation was longer in PD than control subjects, and longer in PD subjects when OFF than when ON, as shown by the examples in Fig. 2A, and by the larger values of foot-off latency (Table 1 summarizes statistics). Levodopa speeded up the step preparation from the OFF state ($p < 0.05$), although foot-off latency in the PD ON group remained significantly longer than in control subjects.

Kinematic characteristics of the first step (Fig. 3) were also sensitive to initial stance width, although less sensitive than the APA. Step length (in percent height, mean ± S.E.M.) was 30.1 ± 1% and 32.4 ± 1% ($p < 0.001$) when control subjects stepped from the narrow and wide stance, respectively. Corresponding step velocity (in percent height/s) in control subjects was 43.2 ± 1% (narrow stance) and 48.1 ± 1% (wide stance) ($p < 0.001$). Step characteristics of subjects with PD also slightly, but consistently, increased from narrow to wide stance. For PD OFF, step length (Fig. 3A) increased from 18 ± 2% to 19.5 ± 2% and for PD ON, step length increased from 22.9 ± 2% to 23.8 ± 1% from narrow to wide stance ($p < 0.05$). Step velocity (Fig. 3B) also increased significantly from narrow to wide stance for PD subjects both when OFF (from 26.6 ± 3% to 31.9 ± 3%; $p < 0.05$) and when ON (from 38.7 ± 3% to 41.4 ± 2.6%; $p < 0.05$). Independent of stance

Table 1
Left panel: backward APA magnitude as measured by peak of backward CoP displacement (mean values ± S.E.M. [mm]); Right panel: foot-off latency from APA onset (mean values ± S.E.M. [s])

	Backward APA magnitude		Foot-off latency	
	Narrow stance	Wide stance	Narrow stance	Wide stance
Control subjects	32.4 ± 2.8	39 ± 2.9	0.55 ± 0.02	0.54 ± 0.01
PD subjects OFF	15.7 ± 2.6	18.5 ± 2.7	0.83 ± 0.09	0.87 ± 0.1
PD subjects ON	27.8 ± 3.1	31 ± 2.6	0.69 ± 0.07	0.68 ± 0.04

Statistical differences between stance conditions and groups of subjects are also shown ($^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$).

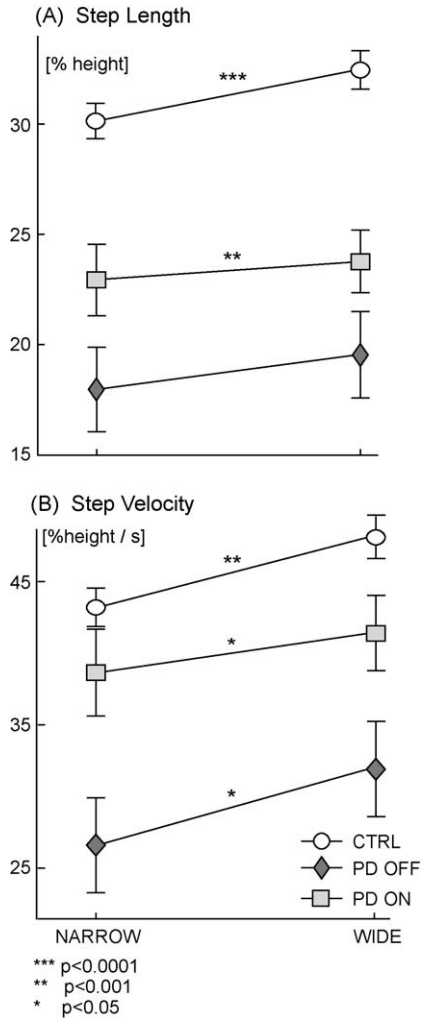

Fig. 3. Kinematics of the first step in narrow and wide stance for control and PD subjects. (A) Step length (mean values ± S.E.M.). (B) Step velocity (mean values ± S.E.M.). $^{***}p < 0.0001$; $^{**}p < 0.001$; $^{*}p < 0.05$.

width, subjects with Parkinson's disease (OFF state) showed smaller step length ($p < 0.0001$) and velocity ($p < 0.001$) compared to control subjects. Levodopa significantly increased the step length and velocity from the OFF state ($p < 0.05$), but, differences between control subjects and PD ON in wide stance remained significant ($p < 0.001$ for step length and $p < 0.05$ for step velocity).

This study showed that preparation for step initiation from wide stance was associated with a larger lateral and backward CoP displacement than from narrow stance. The characteristics of the first step (velocity and length) were also sensitive to initial stance conditions, probably because of differences in the corresponding APA. In fact, previous studies found a linear correlation between lateral CoP displacement and velocity of locomotion [24]. A larger APA was required in wide stance to move the weight off of the initial swing leg, and a larger APA resulted in a longer and quicker step, even when subjects were instructed to step at their natural, comfortable rate for both stance widths in this study. The changes in step characteristics when the APA changed to accommodate an increased biomechanical demand, suggests a close relationship between the program for postural preparation and for stepping.

Basal ganglia deficits resulting from dopamine loss associated with moderate to severe PD did not prevent subjects from scaling their APA for initial stance width, although the magnitude of their APA was less than in age-matched control subjects. PD subjects had much more difficulty initiating a step from a wide stance than from a narrow stance, as shown by the greater differences from control subjects in the magnitude of the APA and by the fact that three PD subjects in the OFF state could not initiate a step at all from wide stance although they could from narrow stance. It is not clear whether PD subjects' increased difficulty in initiating a step from wide stance was due to difficulty in increasing the activation level of muscles for the lateral weight shift due to bradykinesia or was due to difficulty scaling or adapting the APA motor program. Consistent with previous studies, the pattern of step preparation in PD subjects were similar to control subjects, but their movements were characterized by slowness and weakness [2,23,24]. These results could suggest inability to generate appropriate force to execute the movements. Nonetheless, the PD subjects had the ability to produce larger APA when switching to a wider stance, suggesting that they do not lack the ability to produce force, but they seem to underestimate force in relation to initial stance conditions. Consistently, previous studies have shown that PD subjects undershoot targets and poorly scale the magnitude of voluntary arm movements [1,7] and automatic postural responses [15]. These findings were also consistent with previous studies that suggested a role of the basal ganglia in 'energizing' muscle activation for appropriate magnitude of scaling for particular tasks [12].

It has been suggested that the basal ganglia may play a specific role in selecting and adapting motor programs based on initial conditions using proprioceptive input, or in formulating an internal model of body kinesthesia [17]. For example, PD subjects seem to have poor adaptation of postural responses to multidirectional perturbations when the stance width changes [8,14]. They also show poor modulation of postural response magnitude when the support conditions change from a flat surface to a beam, from free stance to a handle support, or from standing to sitting [4], similar to the loss of APA modulation with stance width in our study. The significant relation between disease severity (as quantified by the UPDRS) and magnitude of step preparation but the lack of relation with adaptation from narrow to wide stance suggests that bradykinesia, but not motor adaptation is measured by the UPDRS.

Start hesitation, or freezing at the start of locomotion, is notoriously difficult to quantify because it is very context dependent. None of the subjects in our study actually showed freezing, as lack of a step during the study, although many showed freezing when walking up to the platform and through the laboratory door when in the OFF state. This lack of freezing may be because of the visual cues on the floor, increased attention during the study, or due to the experimenter's instruction to "step whenever you are ready", even though great care was paid to avoid explicit cue or trigger to step in order to evaluate self-initiated and self-paced

steps. The several hundred-millisecond delays in step initiation from onset of APA, combined with smaller than normal postural weight shifts in our PD subjects, could be the basis for start hesitation, and eventually, freezing.

We thought that the likelihood of a PD subject's freezing when attempting step initiation would increase with stance width, since the differences in step preparation between PD subjects and controls were much larger when PD subjects stood in wide stance (actually only about shoulder width apart in our study). In fact, one of the characteristics of PD gait is their narrow width, despite their significant balance deficits [20]. Our results support the hypothesis that PD subjects maintain a narrow stance as a compensation for their inability to sufficiently increase the size of their lateral APA to allow effective step initiation in wide stance.

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