Full length article

Modulation of anticipatory postural adjustments using a powered ankle orthosis in people with Parkinson's disease and freezing of gait

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ARTICLE INFO

ABSTRACT

Background: Freezing of gait (FOG) during gait initiation in people with Parkinson's disease (PD) may be related to a diminished ability to generate anticipatory postural adjustments (APAs). Externally applied perturbations that mimic the desired motion of the body during an APA have been demonstrated to shorten and amplify APAs; however, no portable device has been tested. In this study, a portable powered ankle-foot orthosis (PPAFO) testbed was utilized to investigate the effect of mechanical assistance, provided at the ankle joint, on the APAs during gait initiation.

Research question: Does mechanical assistance provided at the ankle joint improve APAs during gait initiation in people with PD and FOG?

Methods: Thirteen participants with PD and FOG initiated gait across five test conditions: two self-initiated (uncued) conditions in walking shoes [Baseline-Shoes], and the PPAFO in unpowered passive mode [Baseline-PPAFO$_{Passive}$]; three "go" cued conditions that included an acoustic tone with the PPAFO in unpowered passive mode [Acoustic + PPAFO$_{Passive}$], the mechanical assistance from the PPAFO [PPAFO$_{Active}$], and the acoustic tone paired with mechanical assistance [Acoustic + PPAFO$_{Active}$]. A warning-cue preceded the imperative "go" cue for all the cued trials. Peak amplitudes and timings of the vertical ground reaction forces (GRFs) and center of pressure (COP) shifts from onset to toe-off were compared across conditions.

Results: Mechanical assistance significantly increased the peak amplitudes of the GRFs and COP shifts, reduced APA variability, and decreased the time to toe-off relative to the passive conditions.

Significance: These findings demonstrate the potential utility of mechanical assistance at the ankle joint (with or without an acoustic cue) as a method to generate more consistent, shortened, and amplified APAs in people with PD and FOG.

1. Introduction

Freezing of gait (FOG) is a debilitating symptom that is estimated to affect up to one-half of people with Parkinson's disease (PD) [1]. Symptoms of FOG are defined as brief, episodic absence or marked reduction of forward progression of the feet despite the intention to walk [2]. The severity and incidence of FOG symptoms increase with disease progression, becomes resistant to current pharmacological and neurosurgical treatments, are associated with an increased risk of falls, and a decrease in mobility and quality of life [1,3].

FOG often occurs when attempting to transition from standing to walking (termed start hesitation) [2,4]. In healthy adults, the initiation of the first step of gait is preceded by a sequence of anticipatory postural adjustments (APAs) that accelerate the center of mass of the body forward and towards the initial stance foot and thus contribute to balance equilibrium prior to lifting the step leg off the ground [5,6]. Gait initiation APAs are characterized by increased loading of the initial swing leg, unloading of the initial stance leg and a shift in the center of pressure posterior and lateral towards the swing leg (Fig. 1). In people with PD, APAs are typically reduced in magnitude, increased in duration, and more variable from trial-to-trial compared to healthy adults [7–10]. Impairment in the generation of APA tends to be greater in people with PD and FOG compared to those without FOG, particularly for components in the anterior-posterior direction [11–13]. Reduced
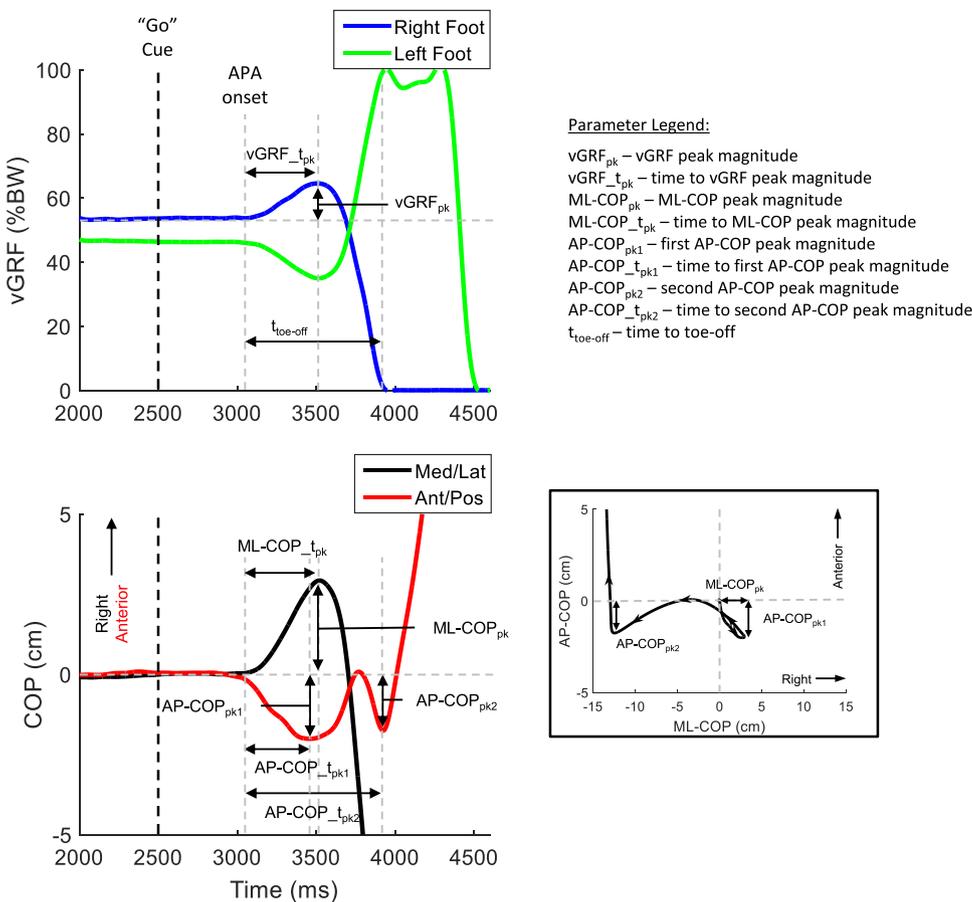
Parameter Legend:

$vGRF_{pk}$ – vGRF peak magnitude
$vGRF\_t_{pk}$ – time to vGRF peak magnitude
$ML\text{-}COP_{pk}$ – ML-COP peak magnitude
$ML\text{-}COP\_t_{pk}$ – time to ML-COP peak magnitude
$AP\text{-}COP_{pk1}$ – first AP-COP peak magnitude
$AP\text{-}COP\_t_{pk1}$ – time to first AP-COP peak magnitude
$AP\text{-}COP_{pk2}$ – second AP-COP peak magnitude
$AP\text{-}COP\_t_{pk2}$ – time to second AP-COP peak magnitude
$t_{toe\text{-}off}$ – time to toe-off

Fig. 1. Illustration of vertical ground reaction forces (vGRF) and center of pressure (COP) during an APA. The inset for the COP data shows the trajectory of the COP underneath the feet in the transverse plane. The nine APA parameters are also included (vGRF and COP): amplitude of and time to peak magnitude from onset ($vGRF_{pk}$, $ML\text{-}COP_{pk}$, $AP\text{-}COP_{pk1}$, $AP\text{-}COP_{pk2}$, $vGRF\_t_{pk}$, $ML\text{-}COP\_t_{pk}$, $AP\text{-}COP\_t_{pk1}$, $AP\text{-}COP\_t_{pk2}$), and time to toe-off ($t_{toe\text{-}off}$). Go-cue is represented as the thick vertical-dashed line at 2500 ms in the time series data.

APA magnitudes contribute to decreased first step velocity [6] and may exacerbate abnormal posture-locomotion coupling that produces start hesitation and FOG [2,7].

Sensory cues (visual, auditory, or somatosensory) can be used to overcome start hesitation and improve gait initiation in people with PD by increasing the magnitude and decreasing the duration of the APAs [7,14,15]. Despite the marked improvements induced by cueing, APAs often remain reduced in magnitude relative to healthy adults [9]. These residual deficits may reflect an impaired capacity to generate force due to reduced muscle mass [16] and/or abnormal muscle activation patterns [17]. Mechanical assistance, applied via translations of the support surface or imposed perturbations of the trunk, can facilitate APA generation and improve gait initiation in people with PD [7,18,19]. An added benefit of these forms of mechanical stimuli is, in addition to mechanical actuation, they induce sensory activation that can act as a cue to further facilitate gait initiation [20,21]. However, a critical limitation of these methods is that they can only be applied in a laboratory setting.

Accordingly, a portable powered ankle-foot orthosis (PPAFO) has been developed to provide untethered mechanical assistance during gait by providing dorsiflexor and plantarflexor torques at the ankle (Fig. 2) [22,23]. This device has been shown to improve APA generation in healthy adults and steady-state gait in people with cauda equine syndrome and muscular dystrophy [23,24]. The purpose of this study was to investigate if mechanical assistance, in the form of a sequence of modest torques applied at the ankle (with or without an acoustic cue), can improve APAs during gait initiation in people with PD and FOG. We hypothesized that, by driving the ankle through the typical dorsiflexor-plantarflexor torque sequence generated during APAs, the PPAFO would shorten APA duration and amplify force production compared with self-initiated (uncued) conditions in people with PD and FOG.

Plantarflexor Torque – Red
Dorsiflexor Torque - Blue

Fig. 2. Experimental set up with the PPAFO attached to the right leg.

2. Methods

2.1. Participants

Thirteen participants with a diagnosis of PD and symptoms of FOG were recruited for this study (9 male, age 66.8 ± 13.4 years, height

170.3 ± 10.8 cm, weight 76.9 ± 15.1 kg). Testing was conducted after overnight withdrawal from Parkinson's medications. Participants were recruited if they reported a score of greater than 1 on item 3 of the Freezing of Gait Questionnaire (FOG-Q) [25,26]. Additional inclusion criteria included: age 45 + years; Hoehn and Yahr rating scale of 2.5–4, no history of musculoskeletal disorders that affect movement of lower limbs; no other significant neurological disorders; able to ambulate independently without use of assistive device (cane, walker) for 50 m in the off-medication state. Exclusion criteria included: history of dementia or cognitive impairment (Mini-Mental Score < 26); clinically significant reductions in vision (when corrected), impaired hearing or cutaneous sensation of the feet; tremor score > 2 on items 20 and 21 of the Unified Parkinson's Disease Rating Scale (UPDRS) in off-medication state; or implanted deep brain stimulators (DBS) or other neurosurgeries to treat PD. The study was performed at the University of Illinois at Urbana-Champaign (UIUC) and the University of Minnesota (UMN). Institutional Review Board approvals were obtained at both institutions, and all participants signed informed consent forms for the study.

2.2. Portable powered ankle-foot orthosis (PPAFO)

Mechanical assistance was provided by a portable powered ankle-foot orthosis (Fig. 2) [22,23]. The PPAFO was capable of providing both dorsiflexor and plantarflexor torque at the ankle through a bi-directional rotary pneumatic actuator (PRN30D-90-45; Parker Hannifin, Cleveland, OH). Two solenoid valves (VOVG and VUVG 5 V; Festo Corp-US; Hauppauge, NY, USA) regulated the flow of compressed gas into each vane of the actuator.

2.3. Gait initiation task

Participants were asked to initiate gait from an upright standing position starting with the right foot across five test conditions. The gait-initiation test conditions were: (1) self-initiated stepping in personal walking shoes [Baseline-Shoes], (2) self-initiated trials wearing the PPAFO, but unpowered [Baseline-PPAFO$_{Passive}$], (3) acoustic go-cue with an unpowered PPAFO [Acoustic + PPAFO$_{Passive}$], (4) mechanical assistance from the powered PPAFO [PPAFO$_{Assist}$], and (5) acoustic go-cue with simultaneous mechanical assistance from the PPAFO [Acoustic + PPAFO$_{Assist}$]. For conditions 2–5, the PPAFO was fit to the test participant (able to fit 4–14 US men's sizes) and worn on the right (stepping) limb (Fig. 2) while their personal walking shoe was worn on the left limb. Blocks of five trials were performed for each test condition (total of 25 trials per participant). The first test condition (Baseline-Shoes) was performed first, followed by conditions 2–5 in randomized order across subjects.

2.4. Cue presentation

For all conditions, the participant was instructed to initiate gait with the right foot "as quickly as possible" and take a minimum of two steps forward. For the self-initiated (uncued) conditions (Baseline-Shoes, Baseline-PPAFO$_{Passive}$), the participant was instructed to stand steady then initiate gait approximately 5–10 s after hearing a ready cue (500 ms, 80 dB, 1 kHz tone). For the cued conditions, an instructed-delay paradigm [27] was used consisting of an acoustic ready cue presented 2.5 s before an imperative go-cue (acoustic tone at 500 ms, 80 dB, 1 kHz) and/or PPAFO mechanical assist [9]. The acoustic ready cue, acoustic go-cue, and actuation of the PPAFO were all controlled with custom software (QUARC, Quanser Consulting Inc, Markham, ON, Canada, and Texas Instruments Code Composer v5, Texas Instruments, Dallas, TX). The mechanical assistance began with a dorsiflexor torque (heuristically tuned to hold the participant's suspended foot at neutral position relative to the shank, i.e., approximately 3–5 N m at 30–50 psig) delivered for 330 ms followed by a subsequent plantarflexor torque of ~9–10 Nm (based on 90 psig actuated pressure) for

83 ms. These timings and patterns of torques were derived from APAs measured in healthy control subjects to encourage a more normative APA profile [9].

2.5. Data collection

Ground reaction forces (GRF), moments, and center of pressure (COP) data were captured using force plates, embedded in the walkway, beneath each foot (Bertec force plates, Bertec Corporation, Columbus, OH at UIUC and Kistler force plates, Kistler Instrument Corporation, Novi, MI, at UMN). Force data were collected at 1000 Hz and filtered using a low-pass Butterworth filter with a cut-off frequency of 20 Hz. The net medial-lateral (ML) and anterior-posterior (AP) COPs were calculated using GRF and moment signals.

2.6. Data analysis

The APAs were quantified using nine parameters derived from the vertical GRF and COP data (Fig. 1). These parameters included the peak magnitudes and times from APA onset for the right vertical GRF (vGRF$_{pk}$, vGRF_t$_{pk}$), ML center of pressure (ML-COP$_{pk}$, ML-COP_t$_{pk}$) and the two posterior peaks of the AP-COP excursion (AP-COP$_{pk1}$, AP-COP_t$_{pk1}$, AP-COP$_{pk2}$, AP-COP_t$_{pk2}$,) (Fig. 1). Vertical GRFs were normalized as a percentage of the participant's body weight. The time from APA onset to right leg toe-off was calculated as the time when the right vertical GRF went below 0.1% of body weight (t$_{toe-off}$). The coefficient of variation (COV) was calculated from all trials within the participant for each parameter (except AP-COP$_{pk1}$ and AP-COP$_{pk2}$). The COV for the two AP COP peaks could not be calculated because these values could be both positive and negative, which invalidates COV.

Onset of the APA was defined as the time when a monotonic change in the signal of greater than three standard deviations was observed relative to the mean signal that was recorded 1000 ms prior to the go-cue. For baseline conditions that did not contain a go-cue, the mean signal was calculated prior to a point manually picked 100–300 ms before vGRF_t$_{onset}$. If there was no monotonic increase in a parameter, the peak magnitude was set to zero and timing was not recorded. All parameters were further verified by visual inspection by a trained researcher.

2.7. Statistical analysis

A one-way repeated-measures multivariate analysis of variance (MANOVA) test was conducted to assess the effect of the five testing conditions on all nine APA parameters. If a main effect was found in the MANOVA, follow up univariate ANOVAs were used to evaluate significant parameters. Separate one-way repeated measures ANOVAs were run for the COV of seven parameters. All p-values reported for COV data are with a Greenhouse-Geisser correction due to violations of sphericity. Post-hoc pairwise effects were examined using Fisher Least Significant Difference (LSD) test. All data were processed using SPSS statistical software (Version 20, IBM Corp, Armonk, NY). Significance level was set to α < 0.05.

3. Results

MANOVA results indicated a main effect of condition ($p < 0.001$). Eight of the nine APA parameters showed significant univariate effects of condition (Table 1). Main effects of condition were also found for the coefficient of variation (COV) of four of the seven parameters. Representative data for each condition are presented (Figs. 3 and 4). These plots exemplify the increase in APA amplitude and decrease in the trial-to-trial variability associated with the cueing, particularly for the mechanical assist conditions.

Table 1

All APA parameters and their coefficients of variation (except for AP-COP$_{pk1}$ and AP-COP$_{pk2}$) across conditions. Significant univariate p-values are bolded, and the superscripts indicate a significant difference from the condition specified (p < 0.05). Data are presented as the average ± s.e.m.

	Baseline Shoes (1)	Baseline PPAFO$_{Passive}$ (2)	Acoustic PPAFO$_{Passive}$ (3)	PPAFO$_{Assist}$ (4)	Acoustic PPAFO$_{Assist}$ (5)	p-value
vGRF$_{pk}$ (%BW)	5.2 ± 1.1[2,3,4,5]	7.8 ± 1.4[1,4,5]	10.4 ± 1.8[1,5]	14.3 ± 1.5[1,2]	15.5 ± 1.6[1,2,3]	**< 0.001**
vGRF_t$_{pk}$ (ms)	322.7 ± 24.9[1]	382.6 ± 27.2[3,4,5]	298.7 ± 24.0[2,4]	237.3 ± 21.1[1,2,3]	289.3 ± 36.4[2]	**< 0.001**
ML-COP$_{pk}$ (cm)	1.5 ± 0.3[3,4,5]	1.8 ± 0.3[3,4,5]	2.3 ± 0.3[1,2,4,5]	3.4 ± 0.4[1,2,3]	3.6 ± 0.4[1,2,3]	**< 0.001**
ML-COP_t$_{pk}$ (ms)	309.4 ± 26.1[2,4]	373.2 ± 28.7[1,3,4,5]	294.1 ± 24.3[2,4]	245.7 ± 10.9[1,2,3]	286.4 ± 36.6[2]	**0.001**
AP-COP$_{pk1}$ (cm)	1.2 ± 0.2	0.9 ± 0.2	1.3 ± 0.3	1.0 ± 0.2	1.3 ± 0.3	0.100
AP-COP_t$_{pk1}$ (ms)	380.4 ± 38.6[3,4,5]	327.7 ± 38.7[3,4,5]	242.4 ± 27.5[1,2,4]	146.5 ± 12.4[1,2,3]	191.0 ± 33.1[1,2]	**0.001**
AP-COP$_{pk2}$ (cm)	1.6 ± 0.6[4]	1.7 ± 0.6[3,4,5]	2.4 ± 0.6[2]	2.8 ± 0.7[1,2]	2.8 ± 0.7[2]	**0.019**
AP-COP_t$_{pk2}$ (ms)	842.7 ± 41.4	846.6 ± 54.2[4,5]	763.4 ± 52.2	709.9 ± 51.3[2]	736.3 ± 57.8[2]	**0.020**
t$_{toe-off}$ (ms)	831.5 ± 50.4[4,5]	866.9 ± 60.5[4,5]	777.9 ± 58.5[4]	671.3 ± 49.0[1,2,3]	695.1 ± 55.2[1,2]	**< 0.001**
Coefficient of Variation (COV)						
vGRF$_{pk}$	0.62 ± 0.11[3,4,5]	0.67 ± 0.16[4,5]	0.34 ± 0.06[1]	0.27 ± 0.06[1,2]	0.26 ± 0.03[1,2]	**0.018**
vGRF_t$_{pk}$	0.29 ± 0.05	0.37 ± 0.06	0.22 ± 0.03	0.30 ± 0.08	0.17 ± 0.04	0.165
ML-COP$_{pk}$	0.57 ± 0.10[4,5]	0.70 ± 0.16[4,5]	0.35 ± 0.06	0.26 ± 0.06[1,2]	0.23 ± 0.04[1,2]	**0.017**
ML-COP_t$_{pk}$	0.28 ± 0.06	0.41 ± 0.08	0.26 ± 0.03	0.27 ± 0.07	0.23 ± 0.05	0.271
AP-COP$_{pk1}$	0.39 ± 0.08	0.45 ± 0.07	0.36 ± 0.04	0.53 ± 0.11	0.27 ± 0.04	0.213
AP-COP_t$_{pk2}$	0.24 ± 0.04[3,5]	0.23 ± 0.04[5]	0.16 ± 0.02[1]	0.18 ± 0.03	0.12 ± 0.02[1,2]	**0.009**
t$_{toe-off}$	0.21 ± 0.04[5]	0.20 ± 0.03[3,4,5]	0.12 ± 0.02[2]	0.13 ± 0.02[2]	0.13 ± 0.02[1,2]	**0.032**

3.1. Vertical ground reaction force

Univariate ANOVAs indicated significant differences in both the magnitude ($F_{4,48}$ = 13.96, $p <$ 0.001) and timing (vGRF_t$_{pk}$, $F_{4,48}$ = 6.80, $p <$ 0.001; t$_{toe-off}$, $F_{4,48}$ = 6.55, $p <$ 0.001) of the vGRF parameters across conditions (Fig. 5, Table 1). Post-hoc tests showed that the vGRF$_{pk}$ was significantly increased in the Baseline-PPAFO$_{Passive}$, Acoustic-PPAFO$_{Passive}$, PPAFO$_{Assist}$, and Acoustic + PPAFO$_{Assist}$ conditions compared to Baseline-Shoes. On average, the cued conditions were associated with a more than two-fold increase in the vGRF. Only the Assist conditions (PPAFO$_{Assist}$, Acoustic + PPAFO$_{Assist}$) showed a significant increase in the vGRF$_{pk}$ compared to Baseline-PPAFO$_{Passive}$. The vGRF$_{pk}$ during the Acoustic + PPAFO$_{Assist}$

condition was also significantly larger than Acoustic-PPAFO$_{Passive}$. The time to vGRF (vGRF_t$_{pk}$) was significantly shorter for all cueing conditions compared to Baseline-PPAFO$_{Passive}$. The PPAFO$_{Assist}$ condition had a significantly shorter vGRF_t$_{pk}$ than Baseline-Shoes and Acoustic-PPAFO$_{Passive}$. Similar to the vGRF_t$_{pk}$ findings, the time to toe-off (t$_{toe-off}$) was significantly shorter for the PPAFO$_{Assist}$ and Acoustic + PPAFO$_{Assist}$ conditions compared to Baseline-Shoes and Baseline-PPAFO$_{Passive}$. The time to toe-off was also significantly shorter in the PPAFO$_{Assist}$ condition compared to Acoustic-PPAFO$_{Passive}$.

There was a significant main effect of condition for the COV of the vGRF$_{pk}$ ($F_{4,48}$ = 5.04, $p =$ 0.018) and t$_{toe-off}$ ($F_{4,48}$ = 10.39, $p =$ 0.032, Table 1). The COV of vGRF$_{pk}$ decreased an average of two-fold for the Acoustic-PPAFO$_{Passive}$, PPAFO$_{Assist}$, and Acoustic + PPAFO$_{Assist}$
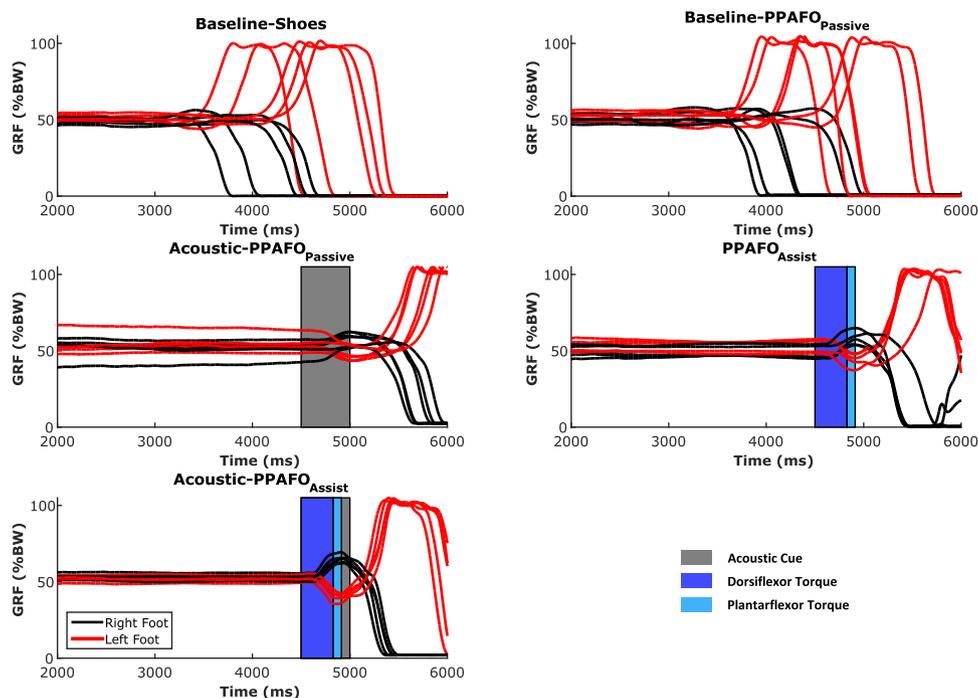

Fig. 3. Representative example of vertical ground reaction force data across all trials and conditions for a participant with PD and FOG.
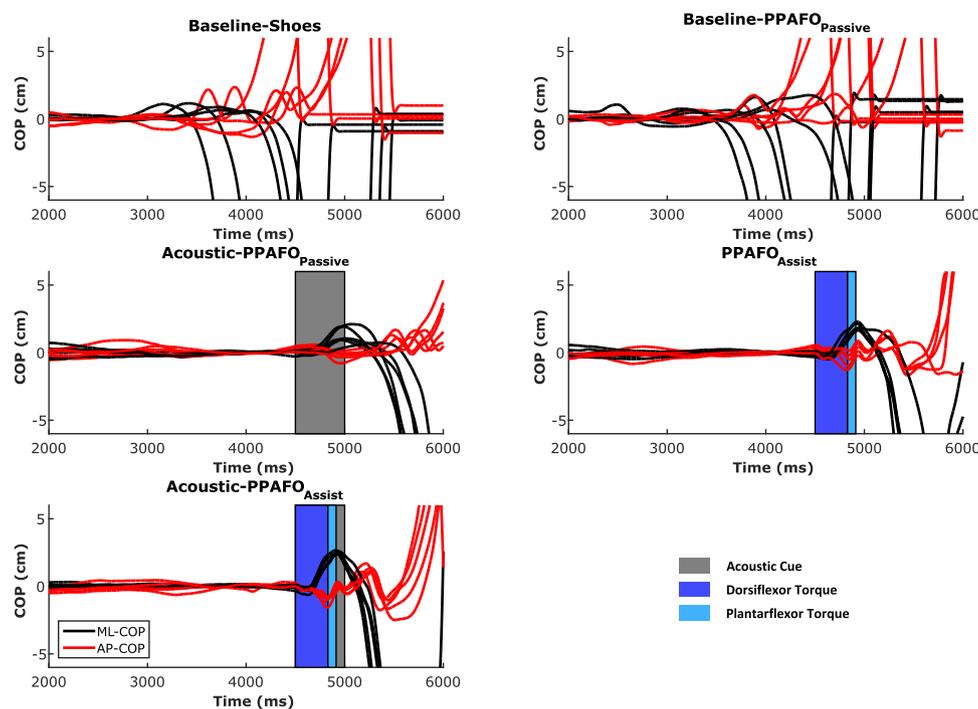
Fig. 4. Representative example of center of pressure data across all trials and conditions for one participant with PD and FOG.

conditions compared to Baseline-Shoes and Baseline-PPAFO$_{Passive}$. Furthermore, both the PPAFO$_{Assist}$ and Acoustic + PPAFO$_{Assist}$ conditions had significantly reduced COV compared to Baseline-PPAFO$_{Passive}$. Similarly, the COV of the time to toe-off ($t_{toe-off}$) was significantly decreased in all cueing conditions compared to Baseline- PPAFO$_{Passive}$. The Acoustic-Assist condition was the only condition that showed a decrease in COV compared to Baseline-Shoes.

3.2. Center of pressure

A significant main effect of condition was observed in the medial-lateral center of pressure parameters (ML-COP$_{pk}$, $F_{4,48} = 16.61$, $p < 0.001$; ML-COP_t_{pk}, $F_{4,48} = 5.49$, $p = 0.001$, Table 1). Post-hoc analyses revealed significant increases in ML-COP$_{pk}$ for the cued conditions (Acoustic-PPAFO$_{Passive}$, PPAFO$_{Assist}$, and Acoustic + PPAFO$_{Assist}$) compared to Baseline-Shoes and Baseline-PPAFO$_{Passive}$. The ML-COP$_{pk}$ was also increased in the PPAFO$_{Assist}$ and Acoustic + PPAFO$_{Assist}$ conditions compared to Acoustic-PPAFO$_{Passive}$. Similarly, the time to reach the peak lateral shift in the COP (ML-COP_t_{pk}) was significantly shorter for the cued conditions compared to Baseline-PPAFO$_{Passive}$. Furthermore, the ML-COP_t_{pk} in the PPAFO$_{Assist}$ condition was significantly decreased compared to Baseline-Shoes. However, a significant increase in ML-COP_t_{pk} was observed in the Baseline-PPAFO$_{Passive}$ compared to Baseline-Shoes.

Univariate ANOVAs also showed a significant main effect of condition for the anterior-posterior center of pressure parameters (AP-COP_t_{pk1}, $F_{4,48} = 11.76$, $p < 0.001$; AP-COP$_{pk2}$, $F_{4,48} = 3.25$, $p < 0.019$; AP-COP_t_{pk2}, $F_{4,48} = 3.22$, $p = 0.020$, Table 1). No significant difference was found between conditions for the first peak amplitude ($p = 0.100$). The time to the first peak amplitude (AP-COP_t_{pk1}) was significantly decreased in all cued conditions (Acoustic-PPAFO$_{Passive}$, PPAFO$_{Assist}$, and Acoustic + PPAFO$_{Assist}$) compared to both Baseline conditions. The timing was further decreased for the PPAFO$_{Assist}$ compared with the Acoustic-PPAFO$_{Passive}$ condition. The second posterior shift in the COP (AP-COP$_{pk2}$) was significantly larger for all cued

conditions compared to Baseline-PPAFO$_{Passive}$. The PPAFO$_{Assist}$ condition also had a larger AP-COP$_{pk2}$ compared to Baseline-Shoes. The time to the second peak amplitude (AP-COP_t_{pk2}) was significantly shorter in both Assist conditions (PPAFO$_{Assist}$ and Acoustic + PPAFO$_{Assist}$) compared to Baseline-PPAFO$_{Passive}$.

The COV of the COP parameters were significantly different across conditions (ML-COP$_{pk}$, $F_{4,48} = 5.08$, $p = 0.017$; AP-COP_t_{pk2}, $F_{4,48} = 3.79$, $p = 0.009$). Mechanical assistance (PPAFO$_{Assist}$ and Acoustic + PPAFO$_{Assist}$) significantly reduced the COV of the ML-COP$_{pk}$ compared to both Baseline conditions. The COV of the AP-COP_t_{pk2} in the Acoustic + PPAFO$_{Assist}$ was also significantly decreased compared to Baseline-Shoes and Baseline-PPAFO$_{Passive}$. Furthermore, Acoustic-PPAFO$_{Passive}$ decreased the COV of the AP-COP_t_{pk2} compared to Baseline-Shoes.

4. Discussion

Findings from this study demonstrate that the mechanical assistance provided by the PPAFO was associated with more consistent, amplified, and shortened APAs in people with PD and FOG. These results are consistent with previous studies showing that externally imposed mechanical assistance, designed to mimic the desired motions of the body during an APA, can improve gait initiation in people with PD [7,18,19]. Our results further demonstrate that mechanical assistance, using a portable device that mimics the kinetics and timing of the ankle dorsi-plantar flexor sequence, can help counteract the diminished and prolonged APAs associated with gait initiation PD.

Mechanical actuation at the ankle had different effects on the early and late phases of the APA. Despite the imposition of a dorsiflexor torque at the ankle, the PPAFO did not significantly increase the magnitude of the initial posterior shift in the COP (AP-COP$_{pk1}$). The lack of increased AP-COP$_{pk1}$ with dorsiflexion assist could have been due to the plantarflexor torque turning on too early in the APA sequence and inhibiting the initial posterior COP excursion (Fig. 4). In contrast, the second posterior shift (AP-COP$_{pk2}$) that occurs near toe-off

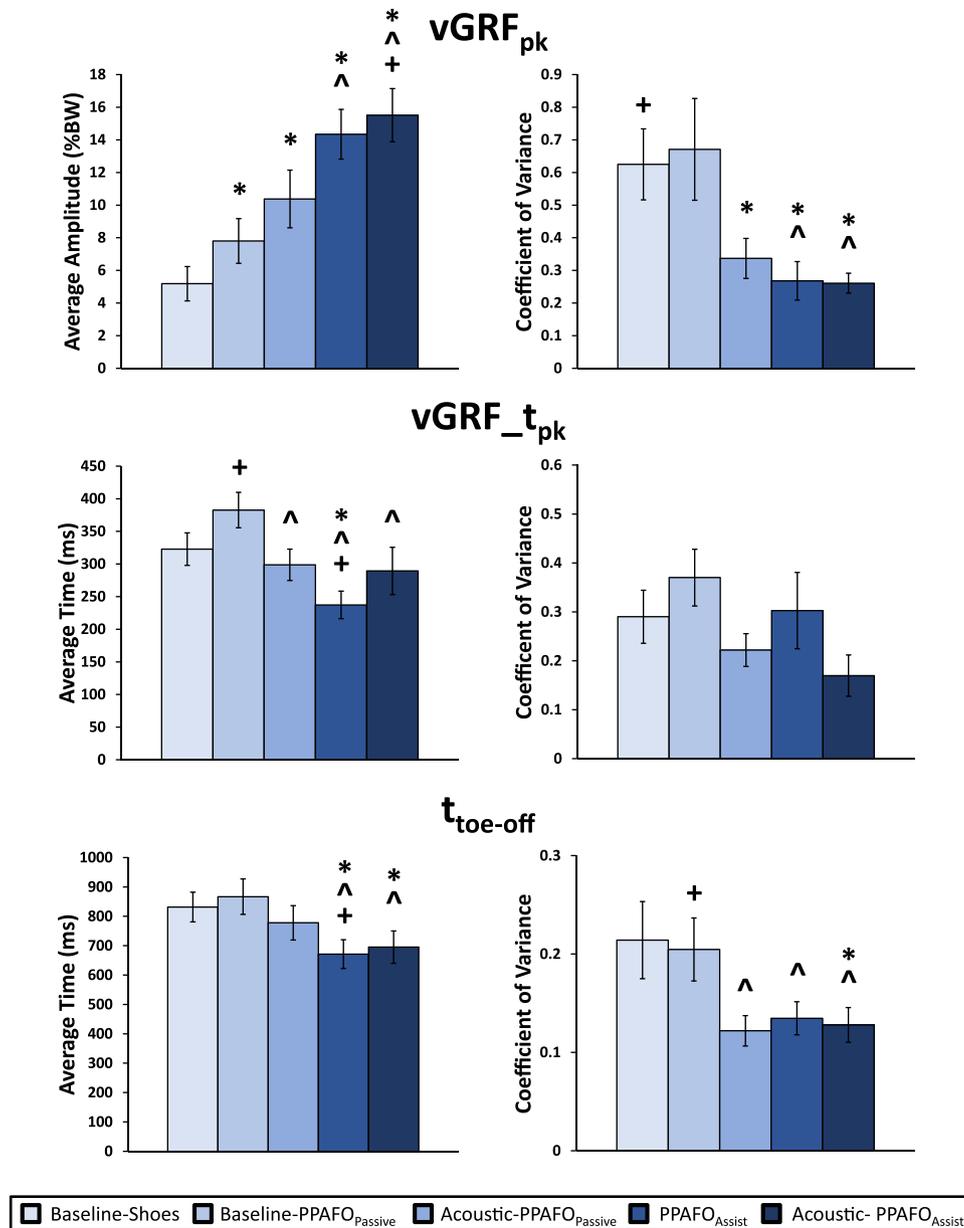**Fig. 5.** Average magnitude (or timing) and coefficient of variation (± s.e.m) for $vGRF_{pk}$, $vGRF\_t_{pk}$ and $t_{toe-off}$. Significant differences ($p < 0.05$) compared to (*) Baseline-Shoes, (ˆ) Baseline-PPAFO$_{Passive}$, (+) Acoustic-PPAFO$_{Passive}$.

was significantly facilitated by mechanical assistance compared to baseline conditions. It is important to note that the plantarflexor assistance was not being provided around the time of AP-COP$_{pk2}$, suggesting that the mechanical assistance facilitated, rather than induced, the posterior excursion prior to toe-off. Future studies with electromyography may give additional insight into whether this increase in AP-COP$_{pk2}$ was due to increased volitional control. Increasing the AP-COP peak excursion late in the step initiation cycle is particularly important in people with PD and FOG since this component is differentially impaired compared with those without FOG [12] and the amplitude of peak posterior shift is closely related to the initial velocity of gait [6].

Sensory cueing in the form of an acoustic tone or mechanical assistance appreciably reduced the trial-to-trial variability (COV) in both the amplitude and temporal characteristics of gait initiation. The COV observed in the ground reaction force and timing parameters ($vGRF_{pk}$, $t_{toe-off}$) during mechanical assistance conditions was comparable to that seen in healthy adults (~20%) [10]. Increased trial-to-trial variability in

the timing and magnitude of APAs [10] have been reported in individuals with PD and FOG compared to healthy controls and this variability may contribute to disturbances in postural-locomotion coupling, start hesitation, and FOG [2]. Accordingly, reduced APA variability, in conjunction with improved amplitude, may reduce the occurrence of FOG episodes in people with PD. However, this notion needs to be empirically tested in scenarios that consistently induce FOG.

Mechanical assistance either alone or in combination with an acoustic tone produced the highest average amplitudes and lowest variability of the APAs (Fig. 3). Moreover, the peak amplitude of the vGRFs and ML-COP were significantly larger with combined mechanical assistance and acoustic cueing, demonstrating that mechanical actuation of the ankle joint added to the benefits produced by sensory cueing alone. These results are consistent with a study showing that paired sensory stimuli was associated with improvements in gait and freezing of gait questionnaire (FOG-Q) scores after a two-week period of in-home training [28].

A limitation of our study was that the duration of the dorsiflexor torque (330 ms) and plantar flexor torques (83 ms) were same across all subjects. As noted above, the onset of the plantar flexor torque may have interfered with the generation of the first posterior shift in the COP. Studies using a medial-lateral waist pull during gait initiation have shown that both the timing, magnitude and direction of the perturbation can have a significant influence on the generation of APAs [29]. For this reason, it is possible that a more individualized approach to programming the amplitude and durations of the dorsi and plantarflexor torques may have improved the results further. Moreover, testing different torque combinations (either faciliatory or inhibitory) may provide insight into any positive learning or retention effects that would prevent reliance on the assistance after long-term daily wear.

5. Conclusions

Mechanical assistance provided at the ankle joint was associated with amplified, shorter duration and more consistent APAs in people with PD and FOG. Furthermore, the pairing of an acoustic cue with mechanical assistance may provide further improvements in APAs and stepping. Future investigation is needed to better understand the mechanisms underlying these changes and how to optimize the assistance.

Conflict of interest

Elizabeth Hsiao-Wecksler is a co-inventor of a US patent for the PPAFO device. This patent has not been licensed to any company or organization.

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