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Anticipatory postural responses prior to protective steps are not different in people with PD who do and do not freeze

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Abstract

Background: Protective stepping after a loss of balance is related to falls. Anticipatory postural responses (APAs) prior to protective stepping can impact step performance, may be larger in people with PD, and have been suggested to be related to freezing of gait (FOG). However, whether people with PD and FOG (PD+FOG) exhibit larger APAs than people with PD and no FOG (PD-FOG) is unknown.

Research Question: Determine the impact of freezing status on APAs prior to protective steps, thus providing a better understanding of the link between FOG and APAs.

Methods: Twenty-eight people with PD (13 PD+FOG) were exposed to 50 support surface translations (25 forward, 25 backward, random order) resulting in protective steps. The size of medio-lateral weight shifts prior to the protective step (i.e. APAs), and the percentage of trials with an APA were calculated via force-plates. FOG status was assessed at the time of testing as well as 3.25(±0.43) years later. Participants without FOG at testing, but with FOG at follow-up were identified as “converters”.

Results and Significance: For both forward and backward protective stepping, size and percentage trials with an APA were not statistically different between PD+FOG and PD-FOG, even after excluding converters from the PD-FOG group ($p>0.27$ for all). No group by direction interactions were observed. These data suggest that, in mild to moderate PD, an inability to couple APAs with stepping, rather than an inappropriately sized APA, may be most related to freezing of gait.

Keywords

Freezing of Gait; anticipatory postural responses; protective stepping

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INTRODUCTION

Anticipatory postural adjustments (APAs) prior to voluntary steps are small in people with Parkinson's disease (PD), leading to ineffective steps[1]. *Protective* steps are quick movements in response to a loss of balance, and are critical for fall prevention[2]. Interestingly, unlike voluntary stepping, APAs prior to protective stepping may be larger than normal in people with PD[3–5].

Recent work suggests a potential link between large APAs during protective stepping and “start hesitation”, a form of freezing of gait (FOG)[3, 6]; as people with PD who freeze (PD+FOG) exhibit larger APAs compared to healthy controls during protective stepping[3]. These larger APAs may be related to an inability to either trigger a step or effectively couple the APA and the step. However, the relationship between FOG and APAs is incompletely understood. Although people with PD+FOG exhibit larger APAs during protective stepping compared to healthy adults[3, 4], it is unknown whether they exhibit larger APAs compared to people with PD who do not freeze (PD-FOG). Therefore, the larger protective-step APAs observed previously may be due to PD progression generally, rather than freezing status. Finally, although postural stability is particularly affected in the backward direction in people with PD[7], APAs during protective backward steps have not been characterized in those with PD.

The purpose of this study was to further characterize the relationship between FOG and APAs during protective stepping by measuring APA size in people with PD+FOG and PD-FOG prior to forward and backward protective steps. Understanding the relationship between APAs and FOG may inform treatment strategies aimed at reducing postural instability and falls in people with PD. Such information is particularly important given the challenges associated with fall prevention in people with PD[8].

METHODS

Participants:

A convenience sample of twenty-eight people with PD participated. Inclusion criteria were: ability to stand without aid for longer than 1 hour, currently taking levodopa, and devoid of orthopedic or neurological conditions (other than PD) affecting balance. Thirteen of 28 participants self-reported FOG via the New FOG Questionnaire (NFOG-Q)[9]. To better characterize freezing status, participants who self-reported as PD-FOG were contacted 3.25(SD=0.43) years later, and asked if they had experienced freezing in the previous month. Of the original 15 participants in the PD-FOG group, 5 participants “converted” to PD+FOG at re-contact. Disease duration and incidence of falls in the previous 6 months were larger in PD+FOG compared to PD-FOG (Table 1). All participants were consented as outlined by the Declaration of Helsinki.

Protocol:

As described previously[5], participants stood with feet 2cm apart on hydraulically driven movable force-plates. First, 12 perturbation trials of varying size and direction were administered to orient participants to support-surface translations. Then participants

underwent 50 trials in which the ground was quickly (15cm, 56cm/s) and randomly moved forward (25 trials) or backward (25 trials) underfoot, resulting in a protective step.

Data collection and analysis:

Ground reaction force (collected at 480Hz) was used to calculate COP during perturbations. COP data were low-pass filtered at 20Hz using a 4th order butterworth filter. Custom Matlab code identified inflection points in medio-lateral movement of the COP, and these points were used to calculate COP displacement[2].

Our primary outcome was the APA size, identified as the largest medio-lateral COP deviation toward the swing foot between 75ms after the perturbation and foot off[2, 3]. For consistency with previous literature[3, 4], we also dichotomized each trial for the presence or absence of an APA, defined as a medio-lateral COP displacement ≥ 4 mm toward the swing limb[2]. The percentage of trials in which at least 1 APA occurred was calculated for each participant. Anterior-posterior (AP) support surface movement precluded assessment of anterior-posterior APAs.

Statistics:

APA size data were $\log_{10}$ transformed to remove skewness (Shapiro-Wilk Test before and after transformation: $p < 0.001$ and $p > 0.24$, respectively). Repeated measures ANCOVAs were used to determine the effect of group (PD+FOG, PD-FOG) and direction (forward/backward) on APA size and the percentage of trials in which an APA was observed. Disease duration was included as a covariate on all ANCOVA analyses. Statistical analyses were run both with converters included and excluded from the analysis. Bivariate regression analysis assessed the association between FOG severity (NFOGQ) and APA size.

Previous work shows that step characteristics and APA size can change differently in PD+FOG and PD-FOG groups with repeated perturbation exposure[10]. To assess the potential group by time interaction, APA size data were averaged into 5 blocks of 5 trials for forward and backward protective stepping, and a mixed-factorial ANOVA was run to assess potential group, time, and group by time interactions.

RESULTS

For forward and backward stepping, APA size and percent of trials with APA were not significantly larger in the PD+FOG group compared to the PD-FOG group ($p > 0.27$ for all, Table 2, Fig.1). No direction or group by direction interactions were observed for APA size or percentage of trials with an APA. The relationship between FOG severity and APA size was non-significant for forward ($p = 0.21$) and backward ($p = 0.20$) stepping.

APA size became smaller across time for backward stepping, both when converters were excluded and included in the analysis ($p = .031$, $p = 0.001$, respectively). No significant changes across time were observed for forward stepping. Importantly, no time by group effect was observed for any analysis ($p > 0.25$ for all).

DISCUSSION

This study investigated the effect of freezing and perturbation direction on APA size prior to protective steps. APAs prior to protective stepping were not significantly different in people with PD+FOG compared to PD-FOG. This remained true even after removing people who went on to freeze from the PD-FOG group. Further, direction of protective stepping did not impact APA size or frequency.

The neural and behavioral circumstances that lead to a freezing event are incompletely understood. Poorly sized APAs prior to stepping (i.e. too large or too small) could precipitate an FOG event by moving the COP either too far or not far enough prior to a step. However, our data showed that APA size was not statistically different in people who did and did not freeze during protective steps. Similarly, recent work shows that APA size prior to voluntary stepping was not different across PD+FOG and PD-FOG groups[11, 12]. This null result should not be over-interpreted, but the current data do not support the hypothesis that APA size directly precipitates a FOG event. Rather, FOG may be related to poor coupling of the APA to the eventual step, possibly due to an inability to release the step[3]. Recent work suggests that APAs may be adaptable through training[13]. Given the relationship between APAs and step characteristics[4], such approaches may positively impact reactive steps. However, although additional work is necessary, current results suggest that such interventions may not directly impact the incidence of FOG.

Interestingly, despite worse performance during backward stepping compared to forward stepping[7], APAs were not larger in the backward direction compared to the forward direction. This suggests a complex relationship between APAs and stepping performance during protective stepping which warrants further investigation[14].

Several limitations should be noted. First, people with PD+FOG were mild to moderate and, as shown previously[15], FOG events during protective stepping were rare. As FOG becomes more prominent, the size and number of APAs may increase, further differentiating those who do and do not freeze[3]. Second, participants stood with feet together, potentially reducing APA size and across-group differences. Third, a-priori power calculations were not conducted to determine sample sizes necessary to capture across-group differences. Therefore, it is possible that the study is underpowered. Further, given our small sample size, statistical outcomes may be poor estimates of true effect sizes across groups. As such, additional studies with a-priori power analyses will be necessary to more completely understand the FOG-APA relationship. Finally, APA size became smaller over time during backward, but not forward, stepping. Although no Time by FOG+/- interaction was observed, it is important to account for the influence of these sequential-effects. Sophisticated methods (such as multi-level models) would account for the rate of APA adaptation. Furthermore, advanced modelling would allow researchers to measure the association between *rate* of APA adaptation and neurologically relevant variables, rather than just average *magnitude* of the APA.

CONCLUSIONS

APA size and frequency were not statistically different in people who freeze compared to those who do not freeze. Although the freezing group was relatively mild, they did exhibit more frequent self-reported falls. Together, these findings support the hypothesis that, in mild to moderate PD, freezing may not be precipitated by poorly sized APAs.

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Figure 1.

Box plots showing the median, inter-quartile range, and max/min of APA size (A) and percentage of trials with an APA (B) during forward and backward protective stepping. People identifying as freezers at the time of testing (PD+FOG, white bars), those who did not (PD-FOG, grey bars), and those who converted from PD-FOG to PD+FOG over the 3.25 year follow-up period (Converter, dotted bars) are shown.

Table 1.

Participant demographics.

	PD-FOG	PD+FOG	Converter	
	Mean (std)	Mean (std)	Mean (std)	p-value *
N (#female)	10(2)	13(5)	5(1)	0.41
Age (yrs)	66.4 (6.6)	66.4 (8.5)	66.2 (5.4)	1.00
UPDRS-Part III	22.4 (11.4)	29.9 (15.1)	27.7 (13.0)	0.21
MiniBEST	23.6 (3.3)	21.2 (4.8)	22.4 (4.8)	0.18
MoCA	26.3 (3.2)	26.0 (3.3)	29.0 (1.2)	0.83
Disease Duration	5.6 (4.1)	11.9 (6.8)	5.7 (1.9)	0.02
NFOG-Q	--	11.8 (6.4)	--	
Fallers	2/10	6/15	0/5	0.05

UPDRS Part III- Unified Parkinson's Disease Rating Scale Motor Score; MiniBEST- Mini Balance Evaluation Systems Test; MoCA- Montreal Cognitive Assessment, NFOG-Q- New Freezing of Gait Questionnaire.

* P-value represents the PD+FOG - PD-FOG contrast. Bolded values represents significance at the p 0.05 level.

Table 2.

ANCOVA outputs assessing the effects of direction (forward & backward) and group (PD+FOG and PD-FOG) on APA size and percent of trials with an APA (% APA) when converters (Con) were and were not included in the PD-FOG group. Disease duration included as a co-variate for all analyses.

		Performance Mean (sd)		Converters Excluded (10 PD-FOG; 13 PD+FOG)			Converters Included (15 PD-FOG; 13PD+FOG)		
		Forward	Backward	<i>Direction (f_{1,20}; p)</i>	<i>Direction × group (f_{1,20}; p)</i>	<i>Group (f_{1,20}; p)</i>	<i>Direction (f_{1,25}; p)</i>	<i>Direction × group (f_{1,25}; p)</i>	<i>Group (f_{1,25}; p)</i>
APA size (mm)	PD-FOG (n=10) PD+FOG (n=13) Con (n=5)	3.7 (2.5) 6.2(4.9) 5.4(4.8)	3.1(3.7) 7.3(8.8) 8.1(4.7)	1.28; 0.27	0.28; 0.61	1.32; 0.27	0.47; 0.50	0.04; 0.84	0.17; 0.69
% APA	PD-FOG (n=10) PD+FOG (n=13) Con (n=5)	32.7(27.4) 41.6(32.3) 40.8(39.8)	26.9(36.9) 39.2(30.4) 61.3(20.2)	0.12; 0.7	0.02; 0.90	0.08; 0.79	0.05; 0.83	0.21; 0.65	0.07; 0.80