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Does the impaired postural control in Parkinson's disease affect the habituation to non-sequential external perturbation trials?

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Suggested Reviewers:	

Highlights

Point 1: Non-sequential perturbation trials resulted in habituation plateau in both groups

Point 2: A slight and not meaningful delay of habituation was observed in Parkinson's group

Point 3: Patients decreased the center of pressure range quicker due to great value on trial 1

Point 4: We assessed the habituation of postural response from the translation of support-base

Type of Manuscript: Research reports.

Does the impaired postural control in Parkinson's disease affect the habituation to non-sequential external perturbation trials?

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Abstract

Background: How people with Parkinson's disease habituate their postural response to unpredictable translation perturbation is not totally understood. We compared the capacity to change the postural responses after unexpected external perturbation and investigated the habituation plateaus of postural responses to non-sequential perturbation trials in people with Parkinson's disease and healthy older adults.

Methods: In people with Parkinson's disease (n=37) and older adults (n=20), sudden posterior support-surface translational were applied in 7 out of 17 randomized trials to ensure perturbation unpredictability. Electromyography and center of pressure parameters of postural response were analyzed by ANOVAs (Group vs. Trials). Two simple planned contrasts were performed to determine at which trial the responses first significantly habituate, and by which trials the habituation plateaus.

Findings: Older adults demonstrated a first response change in trial 5 and habituation plateaus after trial 4, while for people with Parkinson's disease, the first change occurred in trial 2 and habituation plateau after trial 5 observed by center of pressure range. People with Parkinson's disease demonstrated a greater center of pressure range in trial 1 compared to older adults. Independent of trial, people with Parkinson's disease vs. older adults demonstrated a greater ankle muscle co-activation and recovery time.

Interpretation: Despite the greater center of pressure range in the first trial, people with Parkinson's disease can habituate to unpredictable perturbations. This is reflected by little, to no difference in the time-course of adaptation for all but 2 parameters that showed only marginal differences between people with Parkinson's disease and older adults.

Keywords: Movement Disorders, Balance control, Adaptation, Support-base translation, Center of Pressure.

1. Introduction

Adequate postural response to a balance perturbation is important to avoid falls and involves both predictive and reactive neuromuscular responses (Horak et al., 2005, 1997; Mochizuki et al., 2008). Reactive balance responses are triggered after the perturbation onset, and are modulated by perturbation characteristics as well as the individual's central set (Horak et al., 1997; Mochizuki et al., 2008). Due to the neurodegenerative process, Parkinson's disease (PD) affects the excitatory/inhibitory cortical control impairing reactive postural responses (Park et al., 2015). The most remarkable postural changes in people with PD vs. healthy controls are greater displacement of center of mass (CoM) and pressure (CoP) (Horak et al., 2005), which are likely related to an abnormal modulation of muscle response (Dimitrova et al., 2004a; Horak et al., 2005), reflecting excessive activity of antagonistic muscles and muscle co-activation (Bloem, 1992; Carpenter et al., 2004; Dimitrova et al., 2004b; Horak et al., 1992; Lang et al., 2019).

Impaired neuromuscular control in PD affects the ability to adapt/habituate predictive and reactive postural responses to repetitive postural perturbations (Nanhoe-Mahabier et al., 2012; Smith et al., 2012). The habituation to repetitive perturbations indicates a versatility marker of motor control (Oude Nijhuis et al., 2009; Van Ooteghem et al., 2017), which reflects the capacity of an individual to identify and cope with changing circumstances in an optimal and safe strategy (Chong et al., 2000, 1999; Horak et al., 1997). In postural control studies, habituation is observed as decreased muscle activity and CoM/CoP displacements by repetitive exposure to stimuli (Bloem et al., 1998; Nanhoe-Mahabier et al., 2012).

The current knowledge of habituation to postural perturbation in PD is inconsistent (Bloem et al., 1998; Nanhoe-Mahabier et al., 2012; Visser et al., 2010).

While data suggest that people with PD habituate the postural responses (decrease medial gastrocnemius muscle - MG amplitude) after ~3 trials vs. no habituation in older adults (Bloem et al., 1998), other evidence suggests a similar level of postural habituation (decreases in soleus amplitude and trunk flexion after 8 repeated perturbations) in both PD and older adults (Visser et al., 2010). On the contrary, a delay of the postural response habituation in PD compared with older adults (trials 5 vs. 2, respectively) was observed by a decrease in the CoM displacement (Nanhoe-Mahabier et al., 2012). This delay of the postural response habituation to perturbation in PD is reasonable considering the neurodegenerative process, which affects the capacity to identify relevant stimuli and generate adequate responses based on prior experience (Horak et al., 1997; Nanhoe-Mahabier et al., 2012). In addition to those inconsistent results, prior perturbations were induced by rotation of support-base and were repeated in sequence (Bloem et al., 1998; Nanhoe-Mahabier et al., 2012) or under different conditions of the support-base in the same experiment (translation and rotation) (Visser et al., 2010). It is conceivable that continuous repetition of perturbations would affect the habituation of the postural responses. To the best of our knowledge, it has not yet been examined whether PD can affect the habituation responses to unpredictable and non-sequential perturbation trials, situations more commonly experienced during daily life tasks. Therefore, we aimed (1) to investigate the capacity to change the reactive postural responses after unexpected external perturbation between people with PD and healthy older adults (CG), and (2) to investigate the habituation plateaus of postural responses to non-sequential trials of translations of the support-surface in both people with PD and CG. We hypothesized that both groups habituate the electromyographic (EMG) and CoP parameters, but CG vs. PD would present a more rapid change after unexpected external perturbation and habituation plateaus in fewer trials. We also expected that CG would demonstrate a lower EMG and

CoP activity in reactive postural response (demonstrating better balance recovery) (Nanhoe-Mahabier et al., 2012; Visser et al., 2010). These postural changes would be expected mainly by a decrease in the range of CoP (to avoid the CoP positioning close to the limits of stability).

2. Methods

2.1 Participants

Thirty-seven people with PD (PDG) (diagnoses based on criteria determined by the UK Brain Bank) and twenty CG participated in this study. All subjects had not participated previously in other studies that induced displacement of the support base.

We included people with PD in Hoehn & Yahr scale (H&Y) scores <3, and all individuals over 60 years of age. The exclusion criteria were: (i) cognitive decline (Mini-Mental State Examination – MMSE < 24; (Brucki et al., 2003)); (ii) use of any medication that causes side effects in the balance; (iii) orthopedic, musculoskeletal and/or visual impairments that would affect the performance of the protocol; (iv) presence of any uncontrolled disease that could affect peripheral sensory function (e.g., diabetes); and (v) presence of labyrinthitis. The clinical and postural control evaluations were performed in the "ON" state of the specific PD medication (approximately 1 h after medication intake). The participants signed an informed consent form approved by the research ethics committee of the São Paulo State University at Rio Claro–Brazil (CAAE:52534316.1.0000.5465).

2.2 Clinical Evaluation

PDG was assessed by an experienced researcher using the Unified Parkinson's Disease Rating Scale (UPDRS; Fahn et al., 1987) and the H&Y scale adapted version

(Schenkman et al., 2001). Levodopa Equivalent Dosage (LED) was calculated (Tomlinson et al., 2010).

2.3 Postural Control Evaluation

Participants wore a safety harness and stood with feet side-by-side on a force plate fixed to a translating platform. Participants stood for 17 trials each of 20 s duration, with a resting period of 60 s between each trial to allow the participants to move and avoid prolonged periods of static standing. To guarantee the perturbations were unpredictable, the subjects experienced perturbations (15 cm/s of velocity and 5 cm of displacement in the posterior direction) in only 7 out of the 17 randomized trials; the remaining 10 trials were control trials where no perturbation was experienced. The number of trials with perturbation was chosen because previous studies indicated that the habituation plateaus in people with PD occurs within the first 7 trials (Nanhoe-Mahabier et al., 2012). In these trials, the perturbation was triggered at a random time within 5 to 15 s period of the 20 s stance trial.

2.4 Experimental apparatus and procedures

A Trigno^{TM} Wireless System (Delsys, Inc. Boston, MA, USA – 2000 Hz) and a force plate (AccuGait, Advanced Mechanical Technologies, Boston, MA, USA – 200 Hz) were used to acquire the EMG and CoP parameters, respectively. Trigno sensors were positioned on the biceps femoris (BF), vastus medialis (VM), MG and tibialis anterior (TA) of the dominant lower limb for the posture (CG) and of the most affected limb (PDG – determined by UPDRS items) (Barbieri et al., 2016; Beretta et al., 2015) following the SENIAM recommendations (Hermens et al., 2000).

2.5 Data analysis

The perturbation onset and the EMG were synchronized through an accelerometer (Trigno^{TM} Wireless System – Delsys, Inc. Boston, MA, USA – 148.15 Hz) positioned in the force plate by a time vector. The perturbation start time was determined by the moment at which the acceleration was greater than the mean plus two standard deviations of the baseline.

2.5.1 Analysis of EMG parameters

EMG signals were band-pass filtered (20-450 Hz), rectified, and low-pass filtered (50 Hz) using a dual-pass Butterworth filter. In addition, the system had a rejection rate of 80 db, and the resolution of the A/D board was 16 bits. The onset of muscle activity corresponded to the first point where the value was greater than the mean + 2 standard deviations of the baseline (750 and 500 ms before the perturbation) by at least 30 ms (Cleworth et al., 2016). All points of interest were determined by a semi-automatic algorithm (Cleworth et al., 2016). Temporal aspects of the EMG were measured as the onset latency and the time to peak (TTP) of BF and MG (Cleworth et al., 2016; de Freitas et al., 2010). To analyze the EMG amplitude, the magnitude of muscle activation was calculated by the area below the curve (integral - iEMG) for the reactive period, measured over a 250 ms time-window after the muscle activity onset (de Freitas et al., 2010; Santos et al., 2010) (Fig. 1-a). The iEMG was normalized by the iEMG baseline ($100+(100*((iEMG_{reactive\ period} - iEMG_{baseline})/iEMG_{baseline}))$) (de Freitas et al., 2010). After the normalization, the co-activation of BF/VM and MG/TA pairs were determined through the ratio ($(iEMG_{antagonist}/iEMG_{agonist})*100$) (de Freitas et al., 2010) in the reactive period.

2.5.2 CoP analysis

The CoP onset was determined when the CoP displacement was greater than the mean + 2 standard deviations relative to the baseline. Reactive postural responses were analyzed for a period between the CoP onset and 700 ms post-perturbation (Fig. 1-b). In the reactive period, we analyzed the range and the peak of CoP in the anterior-posterior direction. Temporal aspects of the CoP were measured as the TTP and the recovery time to a stable position (defined as the time interval between CoP onset and the instant when the CoP variability (standard deviation during one second) after perturbation was less than or equal to the CoP variability at baseline (determined one second before perturbation) (Beretta et al., 2019).

INSERT FIG. 1

2.6 Statistical analysis

The statistical analysis was performed using SPSS 21.0. Demographic characteristics were compared through Student's t-test. Analysis of reactive postural response was determined by a two-way ANOVA with Group (PDG x CG) and Trial (1x2x3x4x5x6x7) as factor. Trial main effects or Group by Trial interactions were followed up post-hoc using simple planned contrasts. Contrast 1 was performed to determine the earliest trial where significant changes relative to the first trial were observed (Trial 1 vs. 2-7). Contrast 2 was performed to analyze the moment when individuals reached the habituation plateaus, after which no further significant changes compared to the last trial were observed (Trial 7 vs. Trials 2-6). Post-hoc comparisons using Student's t-test were also applied to significant Group by Trial interactions to compare group differences for Trial 1. Significance was set at $P<0.05$.

3. Results

3.1 Participants' characteristics

Statistical analysis indicated that both groups presented similar demographic and global cognition characteristics (Table 1).

Table 1. Mean and standard deviations of participants' characteristics.

	PDG (n=37)	CG (n=20)	*P*-value
Sex (Male/Female)	17/20	8/12	0.666
Age (years)	70.89±8.36	70.50±5.35	0.831
Body Weight (kg)	70.76±11.69	70.56±10.48	0.949
Body Height (cm)	161.64±9.37	162.19±6.92	0.816
MMSE (0-30)	27.75±2.05	28.65±1.63	0.098
UPDRS III (0-108)	25.41±10.28		
H&Y (stage)	2.0(1-3)		
LED (mg/day)	456.29±318.99		
PD duration (years)	5.03±3.60		

UPDRS=Unified Parkinson's Disease Rating Scale; H&Y=Hoehn & Yahr; MMSE=Mini Mental State Examination; LED=Levodopa Equivalent Dose.

3.2 Reactive postural response

3.2.1 Temporal parameters

ANOVA revealed a Trial main effect for the recovery time ($F_{(6,294)}$=9.619, P<0.001, η_p^2=0.164) (Fig. 2-a), onset latency of BF ($F_{(6,324)}$=7.729, P<0.001, η^2=0.125) (Fig. 2-b) and MG muscles ($F_{(6,318)}$=5.071, P<0.001, η_p^2=0.087) (Fig. 2-c), TTP of CoP ($F_{(6,306)}$=25.314, P<0.001, η_p^2=0.332) (Fig. 2-d), and for the TTP of BF ($F_{(6,306)}$=3.342, P=0.003, η_p^2=0.062) (Fig. 2-e) and MG ($F_{(6,192)}$=4.275, P<0.001, η_p^2=0.118) (Fig. 2-f). Compared to trial 1, all individuals had significantly lower values of the TTP of CoP by trial 2 (P<0.001), recovery time by trial 3 (P=0.028), onset latency of BF and MG in trial 2 (P=0.023) and 4 (P=0.037) respectively, and TTP of BF and MG in trial 3 (P=0.015) and 2 (P=0.001), respectively. Compared to trial 7, all individuals had significantly longer TTP of CoP by trial 2 (P=0.025), longer recovery time by trial 5 (P=0.014), greater onset

latency of BF and MG by trials 2 (P=0.006) and 5 (P=0.021), respectively, and longer TTP of BF by trial 4 (P=0.018). There was a main effect of Group for recovery time ($F_{(1,49)}$=18.890, P<0.001, η_p^2=0.278), indicating a longer recovery time for PDG compared to CG (Table 2). Means of significant parameters are also demonstrated in Table 2 and means of non-significant parameters are presented as supplementary material (Appendix A).

INSERT FIG. 2

3.2.2 Amplitude of EMG and CoP parameters

ANOVA indicated a Group by Trial interaction for the range of CoP ($F_{(6,324)}$=4.466, P<0.001, η_p^2=0.076) (Fig. 3-a) and co-activation of BF/VM ($F_{(6,324)}$=2.366, P=0.030, η_p^2=0.042) (Fig. 3-b). For the first trial analyses, there was a greater range of CoP in PDG vs. CG ($t_{(54)}$=3.549, P=0.001), but no difference between groups was revealed for the co-activation of BF/VM ($t_{(55)}$=-0.142, P=0.888). PDG demonstrated a more rapid change for range of CoP, with the first significant change observed in trial 2 vs. 1 (P=0.005) compared to trial 5 vs. 1 (P=0.035) in CG. CG also presented lower co-activation of BF/VM muscles in trial 6 vs. 1 (P=0.034). In addition, when trial 7 was contrasted with other trials, PDG showed a greater range of CoP in trial 4 (P=0.024) and CG showed a greater range of CoP in trial 3 (P=0.021) and greater co-activation of BF/VM in trial 2 (P=0.026). ANOVA revealed Trial main effect for the iEMG of BF ($F_{(6,306)}$=2.777, P=0.012, η_p^2=0.052) (Fig. 3-c) and iEMG of TA ($F_{(6,288)}$=2.927, P=0.009, η_p^2=0.057) (Fig. 3-d). Individuals presented higher values of iEMG of BF and TA in trials 6 and 2 in contrast to trial 1 (P=0.020 and P=0.026, respectively). In addition, participants demonstrated higher values of iEMG of BF and

TA in trials 6 and 2 compared to trial 7 (P=0.006 and P=0.001, respectively). ANOVA demonstrated Group main effect for iEMG of BF ($F_{(1,51)}$=6.493, P=0.014, η_p^2=0.113) and for co-activation of MG/TA ($F_{(1,54)}$=4.308, P=0.043, η_p^2=0.074). CG vs. PDG presented greater iEMG of BF, and lower co-activation of MG/TA (Table 2). Means of the significant parameters are also demonstrated in Table 2 and means of non-significant parameters are presented as supplementary material (Appendix A).

INSERT FIG. 3

Table 2. Mean and standard deviations of temporal and amplitude parameters of EMG and CoP in reactive postural response for the significant Group by Trial interaction main effect of Group and/or Trial.

		Trials							Group*Trial Interaction	Group Effect	Trial Effect
		1	2	3	4	5	6	7			
Range of CoP (cm)	**PDG**	13.9±3.5	11.8±3.4	10.4±3.3	10.5±3.1	9.9±3.0	9.3±3.4	8.8±2.7	PDG:1>2[a];4>7[b]	---	---
	CG	10.7±2.6	11.0±2.4	10.2±2.7	9.4±2.3	9.0±2.4	8.4±2.1	8.4±2.0	CG:1>5[a];3>7[b]		
TTP of CoP (ms)	**PDG**	519.4±86.2	441.2±86.0	425.2±71.4	411.5±81.0	426.1±76.2	406.4±65.1	396.7±73.1	ns	ns	1>2[a]
	CG	518.5±97.0	391.0±81.0	384.0±95.6	399.5±82.6	388.5±72.3	403.0±70.9	384.0±53.5			2>7[b]
Recovery time (s)	**PDG**	3.8±1.0	3.3±0.8	3.3±0.9	3.1±0.8	3.2±1.1	2.8±1.0	2.7±1.0	ns	PDG>CG	1>3[a]
	CG	3.1±0.7	3.1±1.0	2.8±1.3	2.5±0.6	2.3±0.7	2.2±0.9	2.0±0.7			5>7[b]
Onset latency BF (ms)	**PDG**	243.3±172.3	191.1±97.0	186.1±76.1	186.4±86.8	169.2±56.4	168.3±46.1	155.3±57.4	ns	ns	1>2[a]
	CG	249.0±134.2	193.5±71.3	153.5±39.1	173.0±33.9	171.0±49.1	173.0±30.6	166.5±31.3			2>7[b]
Onset latency MG (ms)	**PDG**	179.4±57.6	150.3±45.3	146.1±47.5	143.1±55.8	142.2±41.7	126.1±22.8	124.7±34.7	ns	ns	1>4[a]
	CG	134.2±59.7	143.7±44.0	140.0±50.2	126.8±31.6	131.1±35.3	125.3±32.7	116.3±33.2			5>7[b]
TTP of BF (ms)	**PDG**	233.8±175.5	208.1±198.0	185.9±186.3	183.8±175.0	204.3±139.1	178.4±171.3	152.2±136.0	ns	ns	1>3[a]
	CG	254.4±172.1	212.5±192.3	136.3±87.6	201.3±138.5	102.5±88.1	144.4±91.8	93.8±59.0			4>7[b]
TTP of MG (ms)	**PDG**	296.4±289.5	255.9±314.8	206.4±220.2	147.0±151.7	145.0±135.4	142.7±134.1	183.2±228.7	ns	ns	1>2[a]
	CG	358.3±254.1	110.0±80.9	110.0±80.1	167.5±227.0	154.2±125.9	85.0±50.9	207.5±248.1			ns
iEMG BF (% baseline)	**PDG**	393.0±304.4	401.1±297.4	365.9±278.7	346.0±216.0	380.3±407.2	424.8±361.7	360.8±297.6	ns	PDG<CG	1<6[a]
	CG	591.6±525.8	656.8±656.0	635.1±582.4	514.6±298.2	766.3±511.2	751.0±646.8	631.5±656.6			6>7[b]
iEMG TA (% baseline)	**PDG**	491.5±376.6	582.4±476.8	566.7±561.3	547.1±513.9	474.6±414.5	552.3±558.0	492.6±385.9	ns	ns	1<2[a]
	CG	548.1±593.8	854.8±717.7	420.7±275.7	545.4±361.3	466.2±372.9	399.1±303.7	429.3±355.1			2>7[b]
Co-activation BF/VM (%)	**PDG**	54.1±21.3	55.3±25.2	55.5±23.8	51.0±23.2	54.5±23.6	57.2±26.0	57.3±25.0	PDG: ns	---	---
	CG	56.2±20.3	58.4±24.1	48.5±26.0	45.0±19.0	46.1±28.7	39.3±29.3	43.7±24.9	CG:1>6[a];2<7[b]		
Co-activation MG/TA (%)	**PDG**	61.6±25.5	59.7±25.7	59.1±21.9	52.1±26.0	60.1±24.5	57.7±23.2	57.5±21.2	ns	PDG>CG	ns
	CG	57.8±22.9	53.0±29.1	53.0±32.7	47.3±26.7	50.1±31.5	42.1±24.0	41.5±24.9			

TTP = time to peak; CoP=Center of Pressure; iEMG=integral of electromyography; BF=biceps femoris; VM=vastus medialis; MG=medial head of gastrocnemius; TA=tibialis anterior; PDG=Parkinson's disease group; CG=Control group; ns=not significant; a=indicated the difference in the Contrast 1 analysis; b=indicated the difference in the Contrast 2 analysis. Note: Means of parameters that demonstrated non-significant difference are presented as supplementary material.

4. Discussion

This study investigated the capacity to change the reactive postural responses after unexpected external perturbation between PDG and CG and investigated the habituation plateaus of postural responses to non-sequential trials of external translations of the support-surface in both groups. People with PD present a modest impairment on postural control in situations with external perturbation compared to CG. The greater range of CoP in the first trial and the greater MG/TA co-activation, greater recovery time, and lower iEMG of BF in the unpredictable translation of the support base in people with PD may reflect the central nervous system inability in controlling the muscle activity and in coordinating the muscles in people with PD vs. CG (Bloem, 1992; Dimitrova et al., 2004b; Horak et al., 1992). Indeed, this inadequate muscle control might be associated with the typical rigidity and bradykinesia symptoms in PD, which could impair the balance maintenance, mainly in more challenging situations, such as after external perturbation (Horak et al., 2005; Peterson and Horak, 2016).

The unexpected faster capacity in people with PD to change the postural response after the first trial than older adults (2^{nd} and 5^{th} trials, respectively) is in line with previous data (Bloem et al., 1998). The results may be explained by the 36% higher range of CoP in PDG vs. CG in the 1^{st} trial (indicative of worse postural control to perturbation), which reflects in a greater room for postural adjustments in a subsequent trial (Bloem et al., 1998). However, the worse postural control during the first trial in people with PD needs to be considered with caution because the differences between groups were observed only in the range of CoP.

As expected, both PDG and CG changed postural control when they were exposed to a repeated perturbation, demonstrating an ability to habituate to perturbations. Habituation was observed by a gradual decrease in time to activate muscle (the onset

latency of BF and MG, and TTP of BF and MG), in magnitude of muscle activation (iEMG of TA and BF muscles), and CoP (recovery time to the stable position, TTP, and the range of CoP). The observation that people with PD could modulate and habituate to unexpected and unpredictable perturbation is in line with other studies that demonstrated the capacity of people with PD to change and to habituate the postural response after perturbation (Bloem et al., 1998; Nanhoe-Mahabier et al., 2012). However, previous studies presented the perturbation in blocks (sequence of perturbation trials) and by the rotation of support-base (Bloem et al., 1998; Nanhoe-Mahabier et al., 2012), and a new aspect of our study is that perturbations were presented in non-sequential trials and by the support base translation. One possibility is that the people with PD could somehow retain, at least for a short while, the information from the previous perturbations (Duncan et al., 2014; Van Ooteghem et al., 2017). The postural response adaptations of young adults have been evidenced independently of the perturbation exposure in sequence, suggesting that for the adaptations, the number of perturbations is important (Duncan et al., 2014). The similarities between our data and literature may be related to the characteristics of support-base perturbation, since both types of perturbations required similar involvement of muscle groups and strategies (Duncan et al., 2014; Visser et al., 2010).

Only slight and maybe not meaningful differences were observed in time to habituation plateau in people with PD. Although the delay in habituation in people with PD was expected (Nanhoe-Mahabier et al., 2012), the slight delay in reaching the habituation plateaus needs to be considered with caution since: (a) it was observed in only two parameters (range of CoP and co-activation of the BF/VM); (b) the close difference in these parameters between PDG vs. CG (5th and 4th trials, respectively) for CoP range. While PD impairs the cortico-basal networks and brainstem structures that are responsible for coordinating muscles and for adapting the response to sequential perturbation series

(Nanhoe-Mahabier et al., 2012; Van Ooteghem et al., 2017), people with PD may be compensating for such impairments by using different brain areas (de Kam et al., 2014; Peterson and Horak, 2016). The habituation to repetitive perturbations reflects the individual's capacity to identify and cope with changing circumstances in an optimal and safe strategy (Chong et al., 2000, 1999; Horak et al., 1997). Habituation in few trials could indicate less difficulty, and the adaptation of the postural response (Oude Nijhuis et al., 2009). Thus, it is plausible that procedural learning may have influenced the habituation capacity and may affect the postural response (Duncan et al., 2014; Muslimovic et al., 2007; Nanhoe-Mahabier et al., 2012). Procedural learning supports the idea that the subjects acquire and improve the postural control as the results of repeated perturbation exposures, decreasing the exaggerated responses evidenced during the first trial (Bloem et al., 1998; Nanhoe-Mahabier et al., 2012; Oude Nijhuis et al., 2009). The modest delay in habituation in people with PD may support the idea that, although people with PD demonstrated the ability to retain the improvement of the postural response after practice (Van Ooteghem et al., 2017), procedural learning is less efficient in people with PD than older adults (Krebs et al., 2001; Muslimovic et al., 2007).

Such slight delay in habituation in people with PD is likely linked to the deficits in the basal ganglia function (Jacobs and Horak, 2007; Peterson and Horak, 2016), since this area is associated with learning, control of movements and modulation of postural adjustments (Jacobs and Horak, 2007; Lester et al., 2017; Wilkinson et al., 2009). Such impairments in basal ganglia involve a PD-typical imbalanced excitatory/inhibitory cortical control (Peterson and Horak, 2016; Takakusaki, 2017), impairing the neural drive to synergize and antagonize muscles, which may result in accentuated co-activation during postural control (Papegaaij et al., 2014; Takakusaki et al., 2004). This concept

supports the apparent 19% greater MG/TA co-activation observed in PDG vs. CG (Table 2).

Study limitations include lack of analysis of the perturbation start with the CoP parameters, albeit our protocol allowed us to investigate the temporal and amplitude responses to perturbation by using behavioral (CoP) and control (EMG) strategies. Although the slight delay in habituation plateaus was observed through spatial parameters (range of CoP), additional parameters, such as virtual time to contact (spatiotemporal proximity of the CoP to the limits of stability), would add a greater overview of PD-impairments related to postural response to perturbation (Slobounov et al., 2009, 1997). Also, by selecting a short 250 ms window (same period of the reactive adjustments) to determine the baseline (usual approach adopted by the literature (de Freitas et al., 2010; Santos et al., 2010)), EMG could have had the influence of small bursts of muscle activity. Therefore, future studies should consider longer time-windows (e.g., 500 ms - Cleworth et al., 2016) and include additional analysis to provide more robust information regarding the between-group differences of shapes of postural responses to perturbation over time (e.g., exponential decay functions). Such analysis would detail the group-differences in behavioral aspects of the habituation over time. The difference in postural response between groups in just a few parameters may be explained because our participants with PD are involved in a physical exercise program and because of the lower number of perturbation exposures (Smania et al., 2010). Also, the low number of trials allowed only to identify initial habituation plateaus; thus, future studies with more trials are needed to identify the full habituation of postural responses. Besides, while participants did not know whether a perturbation would or would not occur, they were aware of the direction of the perturbation, which could limit the unpredictability of the task in terms of direction. Future studies should examine the involvement of brain areas during the habituation of

postural adjustments to the perturbation in PD to the neuromechanism and brain networks involved in the task (Jacobs and Horak, 2007, 2006; Mochizuki et al., 2008). In addition, understanding the role of antiparkinsonian medication on postural habituation of people with PD would provide information about the responsiveness of postural response to medication. Despite such limitations, our result could support rehabilitation strategies to improve postural control in PD. Future studies would implement exercise intervention to facilitate the habituation. Furthermore, cue and additional sensorial information could be implemented in those strategies.

5. Conclusions

Despite the greater range of CoP in the first trial compared to healthy older adults, people with PD can habituate to unpredictable postural perturbations. This capacity to habituate is reflected by little, to no difference in the time-course of adaptation for all but 2 parameters (range of CoP and co-activation of the BF/VM) that showed only marginal differences between people with PD and older adults. Therefore, there was only a slight and maybe not meaningful delay to habituate to perturbation in people with PD.

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Figure captions

Fig. 1. Illustration of interest points in the analysis. The figure represents the behavior of a PDG participant in the same trial: a) EMG analysis of MG activity; b) CoP analysis.

Fig. 2. Trial main effect for recovery time (a), onset latency of BF (b) and MG (c) muscles; TTP of CoP (d), BF (e) and MG (f) muscles in reactive postural responses. Note: # Significant difference for trial 1; & Significant difference for trial 7; Solid lines indicate differences in the group by trial interaction and; dashed lines indicate differences in the Trial main effect

Fig. 3. Group*Trial interaction for range of CoP (a) and Co-activation BF/VM (b) and; Trial main effect for iEMG of BF (c) and TA (d) in reactive adjustments. Note: *Significant difference between groups (PDG and CG); # Significant difference for trial 1; & Significant difference for trial 7; Solid lines indicate differences in the group by trial interaction and; dashed lines indicate differences in the Trial main effect

Figure 1

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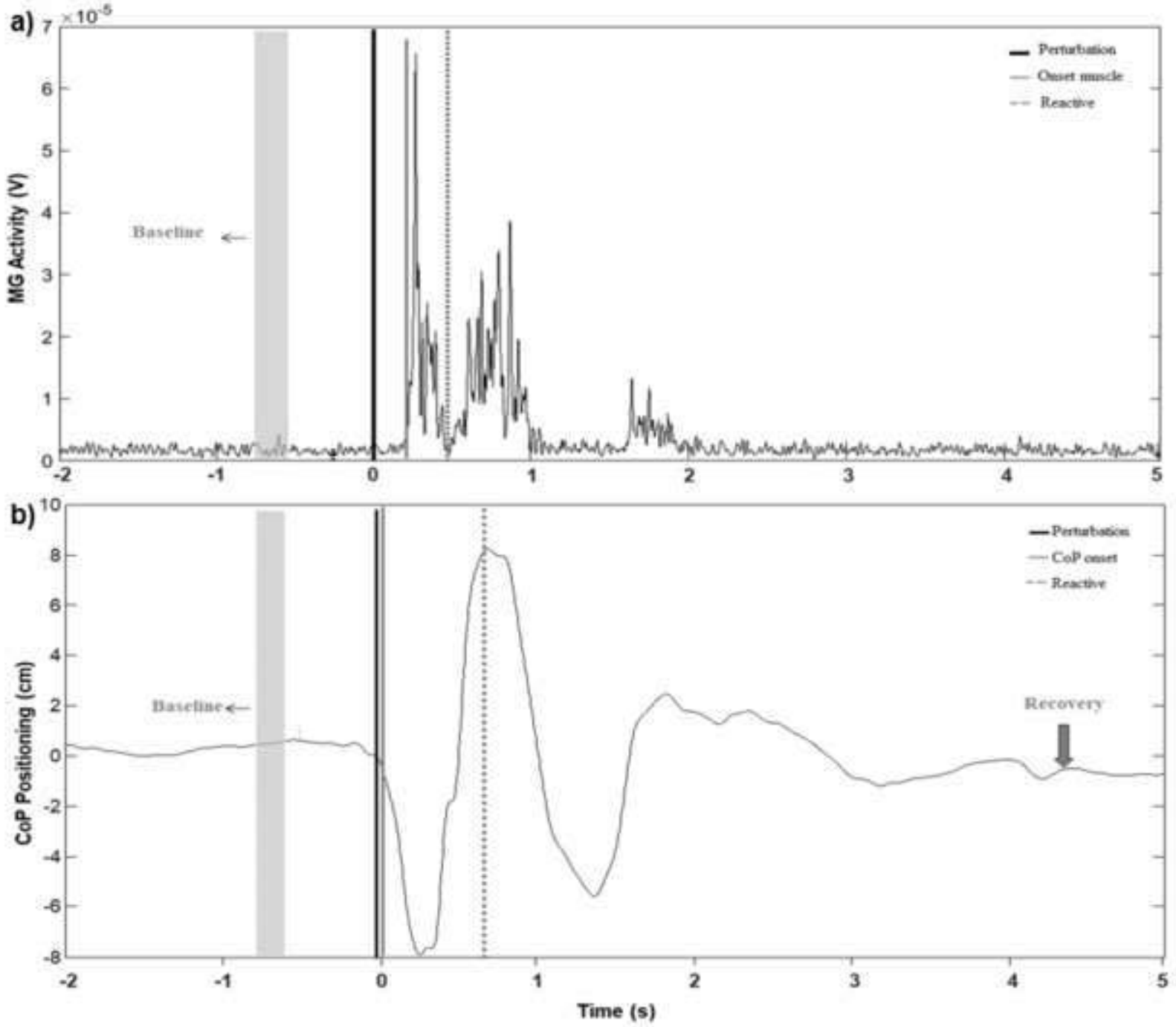

Figure 2

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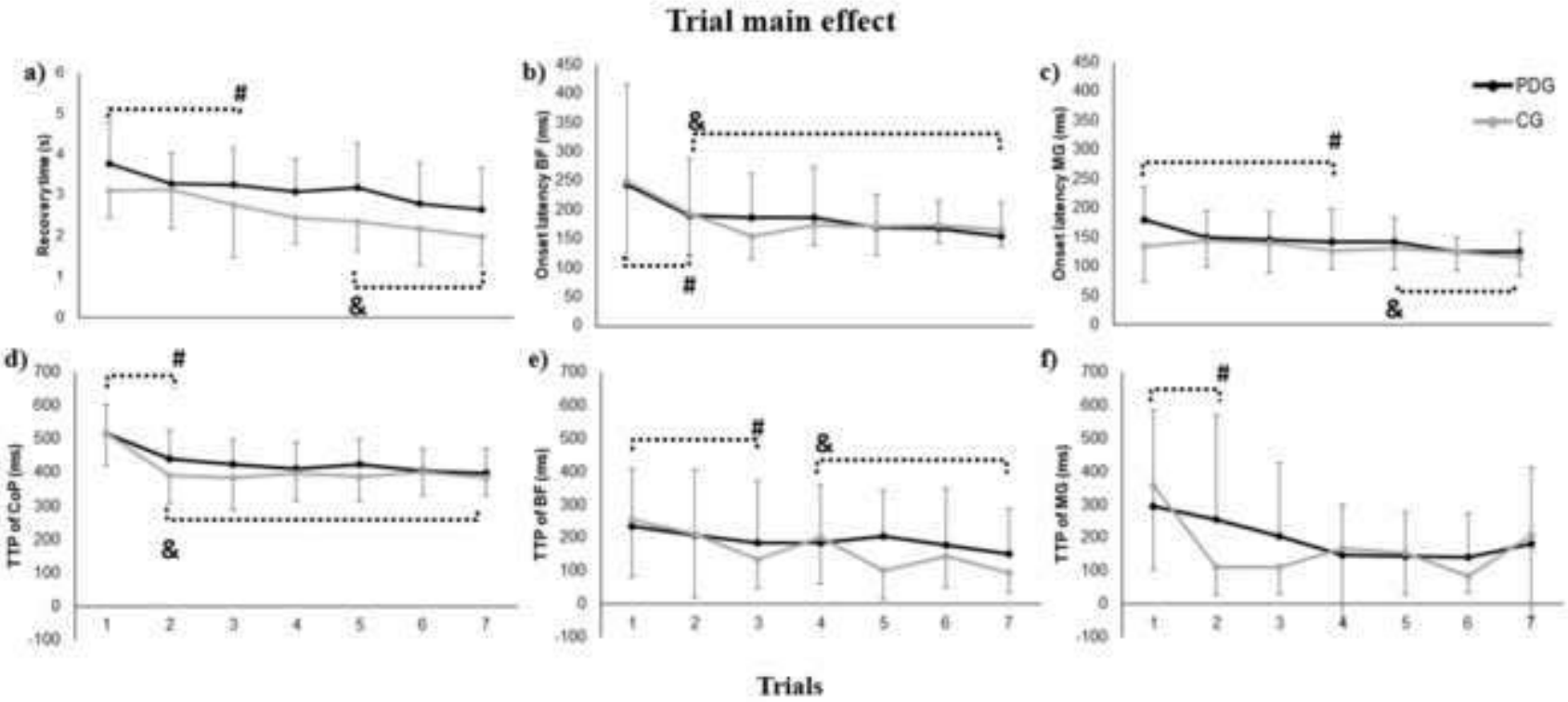

Figure 3

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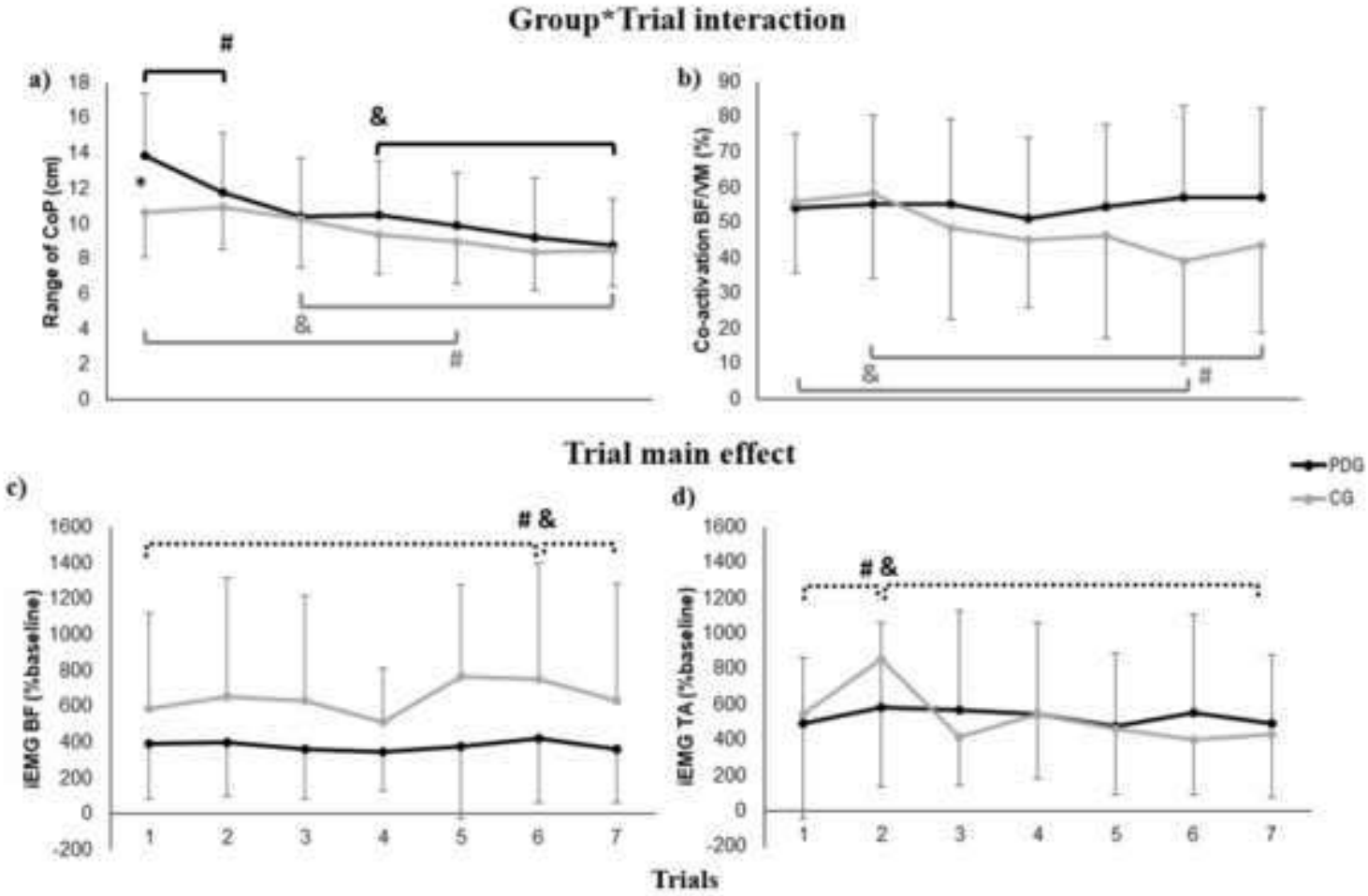

Conflict of Interest

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Supplementary Table S1