



Postural control after unexpected external perturbation: Effects of Parkinson's disease subtype

Victor Spiandor Beretta^{a,b}, Rodrigo Vitória^{a,b}, Paulo Cezar Rocha dos Santos^{a,b,1},
Diego Orcioli-Silva^{a,b}, Lilian Teresa Bucken Gobbi^{a,b,*}

^a São Paulo State University (Unesp), Institute of Biosciences, Posture and Gait Studies Laboratory (LEPLO), Rio Claro, Brazil

^b Post-Graduation Program in Movement Sciences, São Paulo State University - UNESP, Brazil

ARTICLE INFO

Keywords:

Movement disorders
Postural Instability and Gait Disorders
Tremor Dominant
Unexpected disturbance
Reactive adjustments

ABSTRACT

Different clinical subtypes of Parkinson's disease (PD) have long been recognized. Recent studies have focused on two PD subtypes: Postural Instability and Gait Difficulty (PIGD) and Tremor Dominant (TD). PIGD patients have greater difficulties in postural control in relation to TD. However, knowledge about the differences in reactive adjustment mechanisms following a perturbation in TD and PIGD is limited. This study aimed to compare reactive postural adjustments under unexpected external perturbation in TD, PIGD, and control group (CG) subjects. Forty-five individuals (15 TD, 15 PIGD, and 15 CG) participated in this study. Postural perturbation was applied by the posterior displacement of the support surface in an unexpected condition. The velocity (15 cm/s) and displacement (5 cm/s) of perturbation were the same for all participants. Center of pressure (CoP) and center of mass (CoM) were analyzed for two reactive windows after the perturbation (0–200 ms and 200–700 ms). The Bonferroni post hoc test indicated a higher range of CoP in the PIGD when compared to the CG ($p = 0.021$). The PIGD demonstrated greater time to recover the stable posture compared to the TD ($p = 0.017$) and CG ($p = 0.003$). Furthermore, the TD showed higher AP-acceleration peak of CoM when compared to the PIGD ($p = 0.048$) and CG ($p = 0.013$), and greater AP-acceleration range of CoM in relation to the CG ($p = 0.022$). These findings suggest that PD patients present worse reactive postural control after perturbation compared to healthy older individuals. CoP and CoM parameters are sensitive to understand and detect the differences in reactive postural mechanisms in PD subtypes.

1. Introduction

The decrease in dopamine in the basal ganglia, a pathophysiological feature of Parkinson's disease (PD), inhibits the thalamo-cortical motor systems and brainstem and compromises other cerebral structures (Grimbergen, Langston, Roos, & Bloem, 2009; Wichmann & DeLong, 2014). As a consequence, patients present several motor impairments (Takakusaki, Saitoh, Harada, & Kashiwayanagi, 2004), including postural instability (Grimbergen et al., 2009). Furthermore, lesions on the non-dopaminergic nuclei can result in deficits in postural control (Grimbergen et al., 2009). In fact, PD has been recognized as a heterogeneous disease and recent studies have focused on its subtypes according to the different clinical features: Postural Instability and Gait Difficulty (PIGD)

* Corresponding author at: São Paulo State University (Unesp), Institute of Biosciences, Posture and Gait Studies Laboratory (LEPLO), Avenue 24-A, 1515, Bela Vista, 13506-900 Rio Claro, SP, Brazil.

E-mail address: ltbgobbi@rc.unesp.br (L.T.B. Gobbi).

¹ Center for Human Movement Sciences, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.

<https://doi.org/10.1016/j.humov.2019.01.001>

Received 6 June 2018; Received in revised form 20 December 2018; Accepted 2 January 2019

Available online 09 January 2019

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and Tremor Dominant (TD) are the most common subtypes described (Stebbins et al., 2013; Thenganatt & Jankovic, 2014). Patients in the TD subtype present a predominance of tremor symptoms and slower disease progression, while PIGD patients present faster disease progression and late onset, a predominance of bradykinesia and rigidity, and a higher risk of falls (Thenganatt & Jankovic, 2014; van Rooden, Heiser, Kok, Verbaan, van Hilten, & Marinus, 2010) due to postural instability.

Although the differences in postural instability between subtypes of PD have been described through clinical characteristics (Jankovic et al., 1990), there is still a lack of understanding of the differences between subtypes using quantitative assessment (Rocchi, Palmerini, Weiss, Herman, & Hausdorff, 2014). Quantitative posturography has been used to analyze the response after perturbations in people with PD (Dimitrova, Horak, & Nutt, 2004; Horak, Dimitrova, & Nutt, 2005; Nanhoe-Mahabier et al., 2012). These measures have helped researchers and clinicians to better understand the neural correlates of PD-related changes in postural responses (Rocchi et al., 2014). Regarding PD subtype, quantitative evaluation has been used to analyze postural control in quiet standing (Rocchi et al., 2014) and during usual walking and obstacle avoidance (Orcioli-Silva et al., 2018), but not in the reactive postural control following unexpected perturbation. External perturbations are present in activities of daily living, such as bus braking or tripping, and require adequate postural responses to avoid falling. Overall, people with PD demonstrate inflexibility in the Central Nervous System (CNS) in controlling the muscles adequately in situations of external perturbation (Horak, Nutt, & Nashner, 1992), which results in excessive co-activation and lower magnitudes of muscle activity (Bloem, 1992; Dimitrova et al., 2004; Henry, Fung, & Horak, 1998). However, the influence of PD motor subtypes on objective measures of postural response to a perturbation has not yet been fully understood. There is, therefore, a crucial need for additional research in this field. This knowledge will contribute to understanding the specific impairments in postural response according to PD subtype and optimizing the design of rehabilitation programs for each PD subtype.

The aim of this study was to compare the postural reactions following an unexpected external perturbation in TD and PIGD patients and healthy older adults. We hypothesized that PD patients present a longer time to recover the stable position by the difficulty to respond after unexpected perturbation, demonstrating a greater range of center of pressure (CoP) and center of mass (CoM) acceleration in relation to the healthy older individuals. Regarding PD subtypes, the PIGD would have a delay to respond after the perturbation, with longer time to recover the stable position and greater range of CoP and CoM acceleration in relation to the TD. To the best of our knowledge, this is the first study comparing postural control after perturbation in PIGD and TD patients.

2. Methods

2.1. Participants

Forty-five individuals participated in this study. Thirty people with idiopathic PD were selected through a database from a specialized PD center in Sao Paulo state – Brazil, distributed into 2 groups according to the subtype of PD (15 PIGD and 15 TD). For the control group (CG) fifteen neurologically healthy older adults were recruited (Table 1). The diagnosis of individuals with PD was confirmed by expert neurologists, according to the defined UK Brain Bank Criteria (Hughes, Daniel, Kilford, & Lees, 1992) and the patients were on continued use of PD medication. The following exclusion criteria were used: i) PD patients with a score above three on the Hoehn & Yahr scale (i.e. stages 4 and 5); ii) PD patients with indeterminate subtype (ratios between 1 and 1.5 in the subtype classification described in Section 2.2); iii) PD and CG individuals less than 60 years of age; iv) cognitive decline (score < 24 in the Mini Mental State Examination – MMSE – Brucki, Nitrini, Caramelli, Bertolucci, & Okamoto, 2003); and v) musculoskeletal, orthopedic, and/or visual impairments that prevented the subject from performing the required tasks. The individuals with PD performed the assessment in the ON medication state, approximately 45–60 min after taking their dopaminergic medication. The study was approved by the research ethics committee of the São Paulo State University at Rio Claro – Brazil (CAAE: 52534316.1.0000.5465). The participants provided written informed consent to participate in this study.

2.2. Experimental protocol

Clinical evaluation for PD included the motor portion of the Unified Parkinson's Disease Rating Scale (UPDRS) (Fahn, Elton, & UPDRS, 1987) and the Hoehn and Yahr scale adapted version (Schenkman, Wei Zhu, Cutson, & Whetten-Goldstein, 2001). The subtype classification of the patients was performed by the ratio of the mean UPDRS tremor scores (8 items) to the mean UPDRS PIGD

Table 1

Mean and standard deviation of clinical and anthropometric data of the PIGD, TD, and CG.

	PIGD	TD	CG	p-value
Age (years)	69.47 ± 7.69	72.27 ± 7.83	71.60 ± 5.69	0.538
Weight (kg)	72.38 ± 11.83	70.72 ± 10.69	69.91 ± 11.22	0.830
Height (cm)	160.77 ± 10.16	162.53 ± 9.09	161.85 ± 6.49	0.858
MMSE (score)	27.40 ± 1.95	27.93 ± 1.44	28.33 ± 1.75	0.343
UPDRS III (score)	24.67 ± 12.17	25.00 ± 8.83	–	0.932
H&Y (stage)	2.03 ± 0.52	2.07 ± 0.32	–	0.833

MMSE: Mini Mental State Examination; UPDRS: Unified Parkinson's disease Rating Scale; H&Y: Hoehn & Yahr.

scores (5 items). The TD group included patients with ratios equal to or greater than 1.5, while the PIGD group included patients with ratios equal to or less than 1 (Jankovic et al., 1990; Stebbins et al., 2013). Cognitive aspects were assessed using the MMSE (Brucki et al., 2003) in both groups. After this, the individuals were invited to participate in the postural control assessment.

For the postural control assessment, the participants were instructed to stand as still as possible in bipedal stance on a force platform with the feet positioned in the pelvic width distance and eyes fixated at a target positioned approximately 1.5 m in front of them. The force platform was positioned on top of a steel plate, mounted onto a customized electronic/mechanical perturbation platform system. The peak velocity and amplitude of the plate displacement for all participants was 15 cm/s and 5 cm, respectively. These parameters were chosen in order to minimize the chances of evoking a step strategy by the participants (Smith, Jacobs, & Horak, 2014). Postural perturbation was caused by a single translation of the support base in the posterior direction unexpectedly (the perturbation projects the body of the individual in a forward direction). The unexpected perturbation was considered only in the first trial, in which the participant was not informed that the perturbation would occur. To date, the data collection described here is part of a larger protocol assessing the habituation to postural perturbation. For safety, the participants wore a harness during all postural assessments.

2.3. Data analysis

The reactive adjustments were analyzed in two windows: (i) reactive period 1 considered 200 ms after the onset of activity (CoP or CoM acceleration); (ii) reactive period 2 was defined as the time between 200 ms and 700 ms after the onset of activity (CoP or CoM acceleration) (de Freitas, Knight, & Barela, 2010; Henry et al., 1998). An accelerometer (Trigno™Wireless System Delsys, Inc.) positioned on the force platform was used to define the start of the perturbation, which was determined by the moment in which the acceleration was greater than the mean plus two standard deviations of the baseline (period of 2000 ms before the perturbation). The onsets of CoP activity and CoM acceleration were determined as the moments when the signal was greater than the mean by more than two standard deviations of the baseline period (period between 750 and 500 ms before the perturbation).

A force platform – 50 × 50 cm (AccuGait, Advanced Mechanical Technologies, Boston, MA), with a frequency of 200 Hz, was used to obtain CoP parameters. The following outcome measures were calculated: range of CoP (difference between the greater and the lower value of the CoP positioning in each window) in the anteroposterior (AP) direction (Duarte & Freitas, 2010); peak of CoP (maximum value of the CoP positioning after the onset of CoP activity, regardless of time window) in the AP direction; time to peak (time interval between the onset of CoP activity and the maximum value of CoP positioning); and recovery time to stable posture (interval between the onset of CoP activity and the moment of the CoP displacement stabilization, illustrated in Fig. 1). In order to identify the CoP displacement stabilization, a semi-automatic moving-window algorithm routine was developed in Matlab™ (Mathworks, Natick, MA) to determine the instant (first frame) when the CoP variability (standard deviation during one second) after perturbation was minor or equal to the CoP variability at baseline (determined one second before perturbation). The onset of CoP activity (point “A”) and the recovery time (point “C”) are shown in Fig. 1a. Fig. 1b illustrates CoP behavior (reactive response) of one representative participant of each group (PIGD, TD, and CG).

Acceleration of the CoM was measured using a wireless tri-axial accelerometer (Trigno™Wireless System Delsys, Inc.), with a frequency of 148.15 Hz, attached to the 5th lumbar vertebra (Doheny et al., 2012). Peak and the range of acceleration in the AP direction were calculated based on the CoM motion during perturbation.

Statistical analyses were performed using SPSS software (version 21.0) for Windows. The group characterization data were compared through one-way ANOVA to verify the differences between the groups. One-way ANOVA with group factor (PIGD × TD × CG) was applied to verify the differences among groups in the postural response to unexpected perturbation. The significant level was maintained in $p < 0.05$. The Bonferroni post hoc test, with adjusted significance level, was used when group main effect was revealed in the analysis.

3. Results

The statistical analysis did not reveal differences between groups for age or anthropometric and cognitive parameters. Regarding clinical aspects, there were no differences between the PIGD and TD group (Table 1).

For the CoP parameters, ANOVA indicated a significant difference between groups in range of CoP displacement ($F_{2,42} = 4.007$, $p = 0.026$, $\eta^2 = 0.160$) in reactive period 2 postural adjustments and in the recovery time to stable posture ($F_{2,42} = 7.072$, $p = 0.002$, $\eta^2 = 0.252$). The Bonferroni post hoc test indicated greater range of CoP in the PIGD group when compared to the CG ($p = 0.021$, Cohen's $d = 1.185$). In addition, the PIGD demonstrated a longer time to recover the stable position in relation to the TD ($p = 0.017$, Cohen's $d = 0.997$) and CG ($p = 0.003$, Cohen's $d = 1.176$) (Fig. 2).

ANOVA indicated a significant difference between groups in AP-acceleration peak of CoM ($F_{2,42} = 5.219$, $p = 0.009$, $\eta^2 = 0.199$) and in the AP-acceleration range of CoM ($F_{2,42} = 4.043$, $p = 0.025$, $\eta^2 = 0.161$) in reactive period 1 postural adjustments. The Bonferroni post hoc test indicated greater AP-acceleration peak of CoM in the TD compared to the PIGD ($p = 0.048$, Cohen's $d = -0.905$) and CG ($p = 0.013$, Cohen's $d = 1.052$). Furthermore, the TD group showed a greater AP-acceleration range of CoM in relation to the CG ($p = 0.022$, Cohen's $d = 1.258$) (Fig. 3). For the other CoP and CoM parameters, the statistical analysis did not reveal significant differences between groups (Table 2).

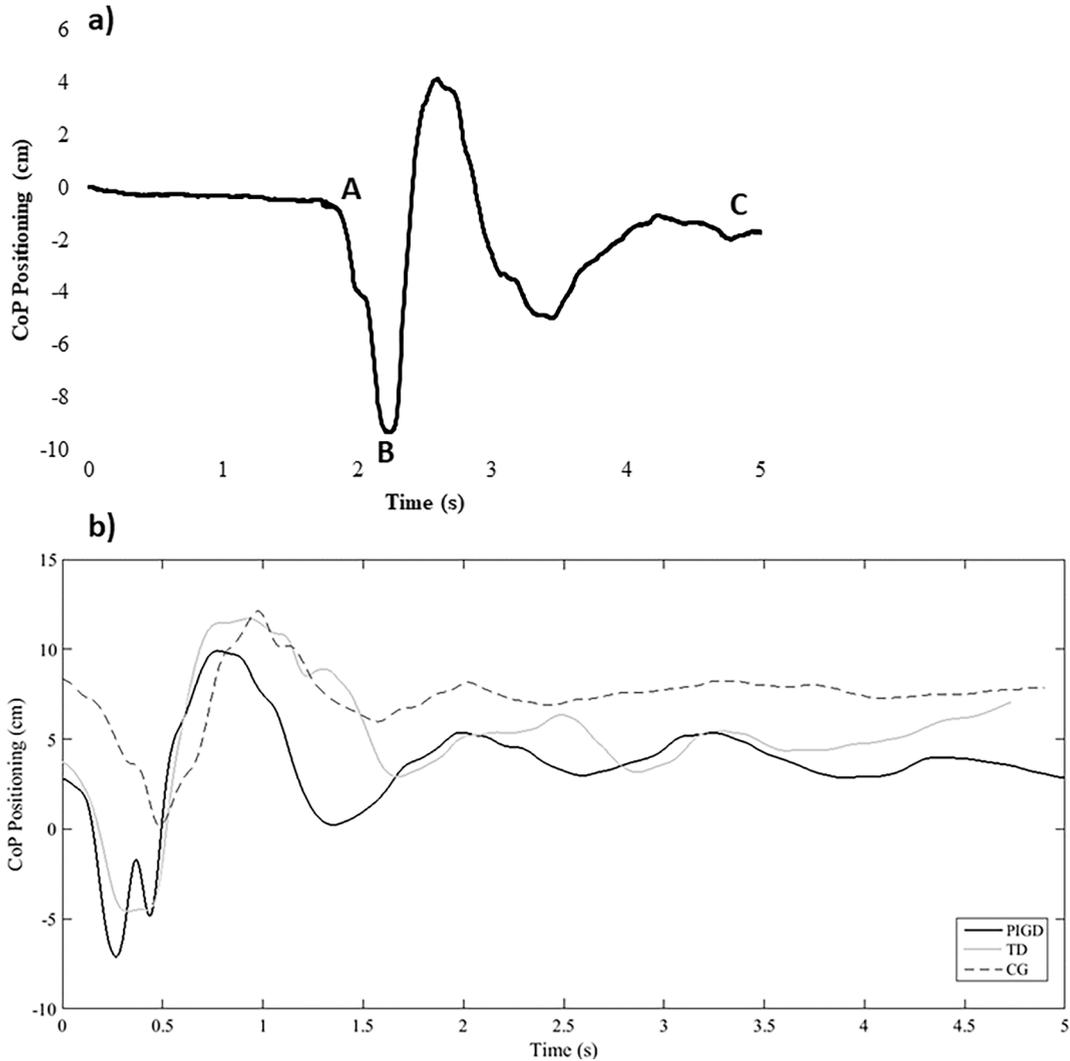


Fig. 1. a) CoP Positioning of a healthy older adult and illustration of interest points. A: Onset of CoP activity; B: The individual response to perturbation; C: Recovery of the stable position; b) CoP behavior (reactive response) of one representative participant of each group (PIGD, TD, and CG).

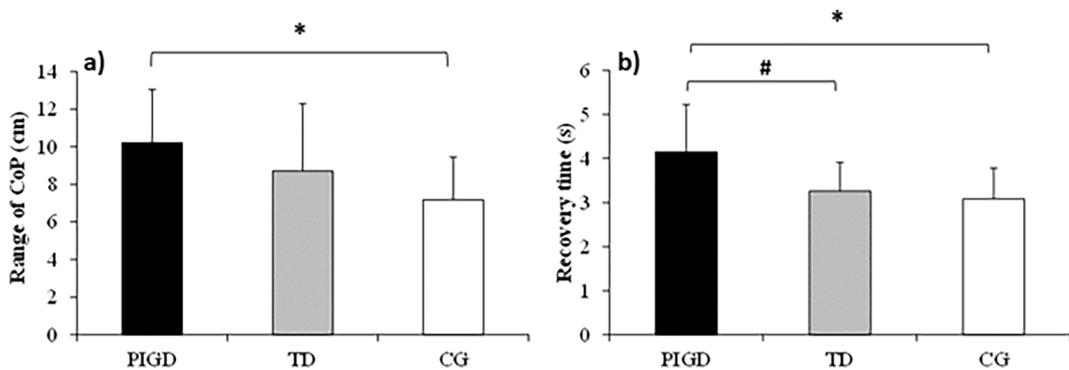


Fig. 2. Mean and standard deviation in the PIGD, TD, and CG: a) range of CoP in reactive period 2 postural adjustments; b) and the recovery time to stable posture. * Significant difference between PIGD and CG; # Significant difference between PIGD and TD.

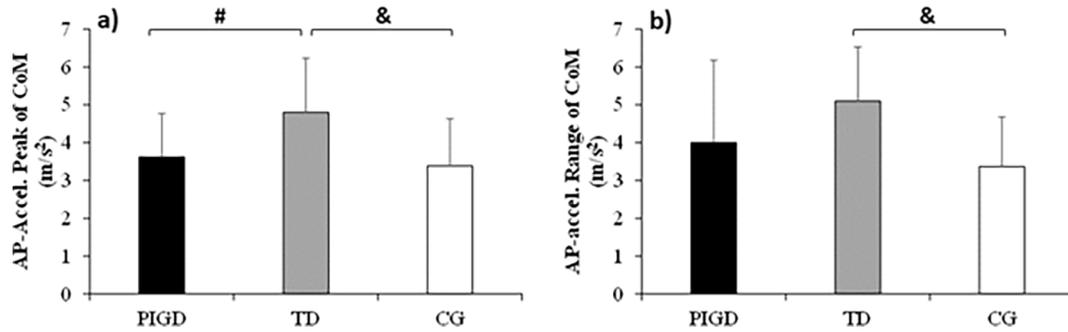


Fig. 3. Mean and standard deviation in the PIGD, TD, and CG: a) of AP-acceleration peak of CoM; b) AP-acceleration range of CoM in reactive period 1. # Significant difference between PIGD and TD; & Significant difference between TD and CG; accel. = acceleration; AP = anterior-posterior.

Table 2

Mean and standard deviation of CoP and CoM parameters of the PIGD, TD, and CG in reactive period 1 and reactive period 2 postural adjustments.

Dependent variables	PIGD	TD	CG	p-value
<i>Reactive period 1</i>				
Range of CoP displacement (cm)	2.49 ± 1.40	2.01 ± 1.28	1.71 ± 0.85	0.213
<i>Reactive period 2</i>				
AP- acceleration peak of CoM (m/s ²)	1.87 ± 1.08	1.79 ± 1.07	1.82 ± 1.15	0.981
AP-acceleration range of CoM (m/s ²)	1.96 ± 1.47	2.00 ± 1.01	1.67 ± 0.81	0.673
Time to Peak of CoP (s)	0.50 ± 0.09	0.53 ± 0.08	0.52 ± 0.10	0.686
Peak of CoP (cm)	7.73 ± 1.51	7.18 ± 1.58	7.18 ± 1.67	0.552

CoP: Center of Pressure; CoM: Center of Mass; AP: anterior-posterior.

4. Discussion

This study aimed to analyze the reactive postural adjustment after unexpected external perturbation in TD and PIGD patients with PD and healthy older adults. The hypotheses were partially confirmed. PIGD patients presented impairment of the postural control in the reactive period 2 while the TD group showed difficulty in control of the posture in the reactive period 1 after external perturbation.

Postural response to unexpected perturbation is impaired in people with PD and influenced by PD subtype. PIGD patients presented longer time to recover the stable position when compared to the TD patients and CG, and a greater range of CoP in reactive period 2 in relation to the CG. TD patients showed a higher AP-peak of CoM acceleration when compared to the PIGD subtype and CG and greater AP-range of CoM acceleration in relation to the CG in the reactive period 1. After perturbation, higher displacement and acceleration of CoM can lead to falls if the reactive response is not adequate (Horak et al., 2005). To date, our results suggest that the adjustments in reactive period 2 are adequate in TD patients. These different responses can be explained by the CNS inflexibility to control the muscles activities adequately and the passive stiffness capacity.

Reactive postural adjustments have been associated with motor impairments characteristic of PD (Bloem, 1992; Horak et al., 2005, 1992). The motor symptoms, especially bradykinesia and muscle stiffness (Bloem, 1992; Horak et al., 1992; Peterson, Dijkstra, & Horak, 2016) which are more evident in the PIGD subtype, are reported to contribute to difficulties in postural control. Patients with PIGD subtype present rigidity signs as a consequence of greater muscle co-activation (Bloem, 1992; Dimitrova et al., 2004; Henry et al., 1998). Increased co-contraction of agonist and antagonist muscles can lead to lower peak and range of CoM acceleration (Horak et al., 2005; Nanhoe-Mahabier et al., 2012). Regarding the observed response in the TD subtype, it is possible that TD patients present a decrease in mechanical stiffness in situations with posture perturbation (since they allowed a higher AP-peak of CoM acceleration in the reactive period 1). Stiffness seems to influence the movement resistance (Boonstra, van Vugt, van der Kooij, & Bloem, 2014; Winter, Patla, Prince, Ishac, & Gielo-Perczak, 1998) by means of muscle tonus properties, reflexive control mechanisms, and muscle co-contraction (Fitzpatrick & Gandevia, 2005; Winter et al., 1998). The increase in mechanical stiffness would decrease sway amplitude and risk of falls (Kang, Quach, Li, & Lipsitz, 2013; Winter et al., 1998), but it is dependent on the context (task) and population (Boonstra et al., 2014; Kang et al., 2013).

Increased stiffness in patients with PD is suggested to lead to difficulty in controlling posture and greater risk of falls (Kang et al., 2013). Our study found that TD patients showed greater CoM accelerations in early reactive responses (passive – reactive period 1), while the PIGD patients and CG presented lower accelerations in this period. However, in the later responses (reactive period 2), PIGD patients needed greater postural adjustments than the TD and CG. In situations with unexpected perturbation, increased mechanical stiffness does not seem to cause as many problems if the reactive system is able to contain and recover the balance in time after the perturbation, which is not evidenced in PIGD. The longer time to recover the stability demonstrated by the PIGD group could suggest a higher risk of falls since this impairment is associated with falls (Beretta et al., 2017). This has implications for activities of

everyday life where unexpected perturbations are common (Visser, Carpenter, Van der Kooij, & Bloem, 2008).

In spite of important findings, some limitations are evidenced. First, the lack of electromyographic analysis hinders a more detailed understanding of motor control. However, this study analyzed the CoP and CoM parameters that are widely assessed in studies with postural perturbation (Horak et al., 2005; de Freitas et al., 2010; Nanhoe-Mahabier et al., 2012). Second, the patients in the present study were in the early and moderate stages of PD, which made it impossible to generalize the results. Third, the unexpected characteristic of perturbation can be considered only in the first trial (Visser et al., 2008). Thus, only one trial of each individual was included in the analysis. With this, the results need to be considered with caution. Nevertheless, studies about unexpected perturbations are very important, since, in daily activities, perturbations are singular and individuals do not know when they will occur. Thus, we suggest further studies involving other types of perturbation and, mainly, involving electromyography analysis for a more complete understanding of the adopted strategy.

5. Conclusion

PD subtypes have a different response after unexpected postural perturbation. TD patients present greater CoM acceleration at the response onset but show no alteration in the later responses (reactive period 2), suggesting that these patients are able to control posture after the imbalance. However, PIGD patients seem to present a more inadequate postural response after the perturbation, remaining in an unstable situation for a longer time than the TD subtype and healthy older adults. Therefore, it can be suggested that CoM and CoP parameters are important to understand the differences in reactive postural control mechanisms in PD subtypes.

Financial disclosures

This work was supported by the São Paulo Research Foundation (FAPESP) [grant number #2016/00503-0] and in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) [Finance Code 001].

Acknowledgment

The authors would like to thank the São Paulo Research Foundation (FAPESP) – Brasil [grant number 2016/00503-0] and the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) [Finance Code 001] by financial support.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.humov.2019.01.001>.

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