# Postural control deficit during sit-to-walk in patients with Parkinson's disease and freezing of gait

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ABSTRACT

*Introduction:* The intricate linkage between Freezing of Gait (FoG) and postural control in Parkinson's disease (PD) is unclear. We analyzed the impact of FoG on dynamic postural control.

*Methods:* 24 PD patients, 12 with (PD + FoG), 12 without FoG (PD-FoG), and 12 healthy controls, were assessed in ON state. Mobility and postural control were measured with clinical scales (UPDRS III, BBS, MPAS) and with kinematic and kinetic analysis during three tasks, characterized by levels of increasing difficulty to plan sequential movement of postural control: walk (W), gait initiation (GI) and sit-to-walk (STW).

*Results:* The groups were balanced by age, disease duration, disease severity, mobility and balance. During STW, the spatial distribution of COP trajectories in PD + FoG patients are spread over medial-lateral space more than in the PD-FoG ($p < .001$). Moreover, the distribution of COP positions. in the transition between sit-to-stand and gait initiation, is not properly shifted toward the leading leg, as in PD-FoG and healthy controls, but it is more centrally dispersed ($p < .01$) with a delayed weight forward progression ($p < .05$). In GI task and walk task, COM and COP differences are less evident and even absent between PD patients.

*Conclusion:* PD + FoG show postural control differences in STW, compared with PD-FoG and healthy. Different spatial distribution of COP trajectories, between two PD groups are probably due to a deficit to plan postural control during a more demanding motor pattern, such as STW.

## 1. Introduction

One of the most severe problems in Parkinson's Disease (PD) is FoG that may occur in up to 60% of patients [1]. It is a serious threat to stability that can produce falls, though a clear relationship between freezing of gait (FoG) and impaired postural control is still unclear. FoG is predominantly triggered in conditions that include dynamic transitional movements, a challenge to postural stability, such as gait initiation or turning [2].

Recently the subtype of PD patients with freezing (PD + FoG) has been characterized by a variety of postural deficits that distinguish these patients by non-freezers. Using a quiet stance position, Nantel and Bronte-Stewart [3] demonstrated that an abnormal increase of centre of pressure (COP) sway amplitude in the medial-lateral direction, is correlated with freezing severity. Delval and colleagues [4] found that during gait initiation freezers are characterized by bradykinetic and hypokinetic Anticipatory Postural Adjustments (APAs). In a detailed analysis of turning, Bengevoord and colleagues [5] revealed a narrow step width in freezers, and other abnormalities in the trajectory of the centre of mass (COM) that impede an adequate postural control. Despite this, more recent studies [6] found no evidences for substantially different postural responses (APAs), measured as COP displacement, during gait initiation, in freezers as compared to non-freezers PD patients. Therefore, the link between postural control and freezing remains a matter of debate.

If balance is impaired in PD patients with freezing, we hypothesize that the increase of motor tasks complexity – through an increase of dynamic postural control demands – would have an effect in the differentiation between the motor profiles of Parkinson's patients with and without freezing, even outside an actual freezing phenomenon. Moreover, given that PD patients with freezing are also impaired in those cognitive domains interacting with gait, and freezing phenomenon have recently been attributed to executive and attentional processes [7,8], we also manipulated the cognitive effort during the motor task.

We investigated postural control abilities in patients with Parkinson's disease, with and without freezing of gait, and in a matched control group, during the execution of three motor tasks: walk, gait

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initiation, and sit-to-walk. These tasks are characterized by different levels of difficulty to maintain postural control. In the most difficult task, sit-to-walk, different components (sit to stand and gait initiation) are merged around the point of seat-off, that is essential to exploit the inertial characteristics of both tasks [9,10]. The preparatory postural phase is strictly related to the stepping phase and is underpinned by a consistent motor switching while maintaining balance. Sit-to-walk is an unstable motion and requires appropriate balance abilities, and a more advanced motor control to govern a forward impulse movement, that the first swing of the leg must inhibit afterwards [11].

We approached the description and analysis of motor differences between patients during walk, gait initiation, and sit-to-walk tasks, by extracting kinematic and kinetic parameters related to anticipatory postural adjustment.

## 2. Materials and methods

### 2.1. Participants

Twenty-four patients diagnosed with PD – according to the UK Brain Bank Criteria [12] – were enrolled from the outpatient clinic for movement disorders at our city hospital. The inclusion criteria were: mild to moderate disease (Hoehn & Yahr ≤3); optimized and stable pharmacological therapy for at least 1 month before enrolment; no cognitive impairment as tested with Mini Mental State Examination [13] (score ≥24). Exclusion criteria were: no other neurological or orthopaedic impairments limiting independent gait; neither Deep Brain Stimulation (DBS), nor Duodopa treatment. Patients were classified as having freezing of gait if their score was ≥1 on the Freezing of Gait Questionnaire (FOG-Q) [14] item 3, and divided in two groups: with FoG (n = 12), and without FoG (n = 12). All patients were assessed in the ON phase, one hour after taking medication; they were matched for motor symptoms severity, gait, and postural control with the following clinical scales: Unified Parkinson Disease Rating Scale – part III [15], Berg Balance Scale [16], Modified Parkinson's Activity Scale [17]. At the testing time, they had no dyskinesia or other type of involuntary movements. Twelve participants, matched for age and Body Mass Index (BMI) with no neurological and motor disorders, also participated in the study. The study was approved by the local ethical committee (University of Trieste; Nr. 70/2016). All participants gave written informed consent.

### 2.2. Experimental design

All participants attended the gait laboratory once, and following mass, height, leg's length measurement, were asked to perform three different tasks: steady-State walking (W); initiation of gait (GI); sit-to-walk (STW). All tasks repeated 5 times were performed, in barefoot condition, along a 10-m walkway surrounded by seven cameras motion capture Qualisys System (120 Hz). Two force plates (AMTI) were positioned in the centre of the trajectory in order to collect dynamic forces acting on the foot during the tasks (120 Hz). Twenty-four retroflective markers were placed over the body according to the modified Helen Heyes marker set [18].

In the W task the participants were asked to walk along the walkway after a verbal go-signal. During GI task the participants stood upright quietly in the centre of the first force plate with both feet for two seconds, and then started walking after the go-signal, taking the first step on the second force plate. Finally, in the STW task the participants were seated on a height adjustable, backless and armless stool (knee angle 100°) positioned just before the first force plate, with their feet placed comfortably in parallel on the platform, and after the verbal go-signal they raised and walk until the end of the walkway. The bench height was adjusted to the subject leg's length. Moreover, feet were placed in the same AP direction with a same comfortable inter-malleolar distance. Potential differences due to upper limbs movement were

**Table 1**
Demographic and clinical[a] characteristics of patients with Parkinson disease (PD) with and without freezing of gait (FoG) and healthy controls.

| | PD + FoG | PD-FoG | Control |
|---|---|---|---|
| | n = 12 | n = 12 | n = 12 |
| Sex, M/F | 8/4 | 7/5 | 6/6 |
| Age | 70.3 (8.9) | 68 (12) | 67.4 (8.7) |
| Disease duration | 9.3 (5.3) | 6 (4) | – |
| Mini Mental State Exam | 27.8 (2.1) | 29 (2) | – |
| Hoehn and Yahr stage | 1.7 (0.5) | 1.5 (0.4) | – |
| UPDRS III | 13 (4.9) | 12 (7) | – |
| Berg Balance Scale | 52.3 (3.9) | 53.1 (3.3) | – |
| Modified Parkinson Activity Scale | 57.5 (6.2) | 60 (4.3) | – |
| Body mass index | 25 (3.2) | 23.7 (3) | 24.9 (3.9) |

[a] Data are mean (SE). UPDRS, Unified Parkinson Disease Rating Scale. Groups were similar by Student *t* test.

**Table 2**
Mean execution times and statistical comparison. (Data from the single task condition only).

| | Execution time (s) | | | Kruskal-Wallis Test PD + FoG vs. PD-Fog vs. Control *p*-value (df = 2) | Wilcoxon-Mann-Whitney Test *p*-value |
|---|---|---|---|---|---|
| | PD + FoG | PD-FoG | Control | | |
| Walk | 1.18 | 1.20 | | 0.347 | 0.603 |
| | 1.18 | | 1.29 | | 0.193 |
| | | 1.20 | 1.29 | | 0.272 |
| Gait Initiation | 1.11 | 1.17 | | 0.443 | 0.326 |
| | 1.11 | | 1.18 | | 0.248 |
| | | 1.17 | 1.18 | | 0.729 |
| Sit-to-Walk | 1.64 | 1.54 | | 0.783 | 0.579 |
| | 1.64 | | 1.51 | | 0.578 |
| | | 1.54 | 1.51 | | 0.686 |

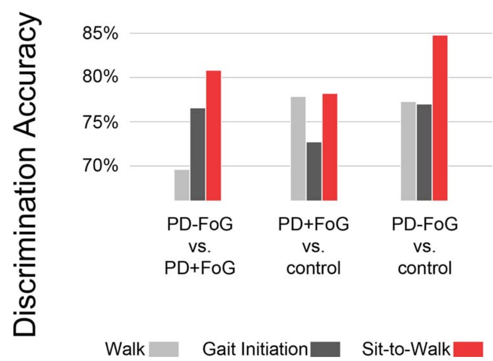


**Fig. 1.** Illustrates recognition performances of LDA algorithm on probe sets of (pairs of group of) participants during the three tasks protocol. LDA procedure: after identification of task – specific significant motion parameters trough ANOVA, only 4 principal components with large eigenvalue were used in the LDA classification algorithm instead of the original variables themselves, solving the collinearity problems and balancing their number between the tasks.

diminished by requiring the participants to sit with the palms of their hands on their waist. All tasks were performed at self-selected rate. During GI and STW the participants were instructed to start the first step with the left limb. In STW we asked participants to have a continuous movement (without pauses) between the sitting, standing and walking phases. In addition, the three motor tasks were performed under single- and dual-task conditions (without or with a concomitant cognitive task). The dual-task condition required attending to an inverse counting of the days of the week, while performing the motor task, as describe elsewhere [19]; the concomitant verbal task was chosen without motor components to avoid direct motor interference to the tasks. It has been established that carrying out a verbal cognitive task during movement markedly increase hypokinesia [20]. Tasks, but not conditions, were randomly assigned to the participants. Before data collection, all participants were asked to practice the tasks.

## 3. Data analysis

### 3.1. Kinematic and kinetic indices

We identified a specific set of indices that characterize postural control: the time and position of both Centre of Mass (COM) and Centre of Pressure (COP) were calculated across the three tasks. In the W-task, the indices were extracted during both left and right leg stance, during two events: at the instant of heel strike, and at toe-off. In the GI-task we analysed the characteristic excursion of the COP before taking a step (imbalance and unloading phases), and during the stepping phase [21]. During the imbalance phase, when the COP shift backward and towards the swinging foot, the indices were extracted at the instant of the maximum COP forward displacement (APA onset, event A), and at the instant of heel-off of the leading foot (event B), when maximum backward shift of the COP occurred. During the unloading phase, the indices were extracted when the COP shift towards the stance foot, at the instant of toe-off of the leading foot (event C). Finally, as for the stepping phase, we identified heel strike of leading foot (event D), and toe-off of the trailing foot (event E). In STW-task, COP and COM times and positions were calculated according to Buckley and colleagues [22]: in the flexion phase at the seat-off event (T1); in the extension phase at the peak vertical velocity (T2); in the unloading phase at the heel-off (T3), and toe-off of the leading foot (T4); in the stance phase at the toe-off of the trailing foot (T5).

### 3.2. Statistical analysis

The analyses were first conceived to quantify the presence of postural control differences among the 3 groups in performing the 3 tasks, and then to pinpoint the nature of these differences in each group.

Firstly, to verify the presence of differences among the three tasks in the participant's postural abilities, we applied a linear discriminant analysis (LDA) algorithm to find a linear combination of task's indices and modelling the discriminatory information between groups. This method is commonly used as dimensionality reduction technique for pattern-classification, and in our case to see if and which of the three tasks discriminate between the groups by finding intergroup classification boundaries on each task to evaluate their motor performance [23]. Particularly, task-specific kinetics and kinematic indices, indicating statistically significant differences between paired groups ($p < .05$), were used as inputs to the LDA classifier. Since the collinearity among input variables could affect the classification ability of the method, a possible solution is the use of Principal Components computed from initial data set [24]. Hence, to avoid multicollinearity, we extracted the first 4 Principal Components (PC) accounting for an average of 84% of the total variance of the indices previously selected. The LDA was then implemented by dividing the participants of the three groups into two sub-groups: the training data (75%), and the test data (25%). All possible training/testing data combinations were generated. Finally, the algorithm performance in the classification task was evaluated averaging accuracy rates on every combination drawn. This first analysis quantifies the discriminatory capacity for each of the three tasks without preselecting indices, and thus keeping the focus on the tasks.

The second analysis is focused to describe the peculiar behaviour of each group in the three tasks. To explicitly analyse postural control differences between participants, we considered the three-dimensional data of COP and COM positions and compared the volumes of prediction ellipsoid [25–29] of each group by means of the Generalized Variance (GV), a scalar measure of dispersion defined as the determinant of the sample covariance matrix and proportional to specific equal-

**Table 3**
Major axe extension in meters of contouring ellipsoid and Chi-square log- Likelihood Ratio Test (log_LRT) indices for pairwise comparisons along all tasks for COP and COM positions.[a] (Data from the single task condition only).

| | COM | | | | | | COP | | | | | | COM & COP | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Major axe extension (m) | | | log_LRT(χ2) Robust MVE | | | Major axe extension (m) | | | log_LRT(χ2) Robust MVE | | | log_LRT(χ2) Robust MVE | | |
| | PD + FoG | PD-FoG | Control | n = 100% | n = 95% | n = 85% | PD + FoG | PD-FoG | Control | n = 100% | n = 95% | n = 85% | n = 100% | n = 95% | n = 85% |
| Walk | 1.263 | 1.323 | | 3.91 | 7.70 | 12.56 | 0.152 | 0.132 | | 4.24 | 3.90 | 2.57 | 4.60 | 3.271 | 4.14 |
| | 1.263 | | 1.348 | 15.83 | 21.61** | 21.16** | 0.152 | | 0.139 | 2.14 | 3.08 | 3.17 | 3.50 | 2.661 | 4.497 |
| | | 1.323 | 1.348 | 12.40 | 12.57 | 9.84 | | 0.132 | 0.139 | 1.88 | 2.99 | 2.64 | 2.44 | 2.118 | 2.041 |
| Gait Initiation | 0.398 | 0.487 | | 4.71 | 4.28 | 4.55 | 0.127 | 0.128 | | 11.44 | 22.44** | 19.09** | 6.42 | 3.00 | 4.77 |
| | 0.398 | | 0.469 | 19.92*** | 18.07** | 16.84** | 0.127 | | 0.148 | 26.31*** | 40.14*** | 37.32*** | 13.30 * | 10.30 | 11.81 |
| | | 0.487 | 0.469 | 9.05* | 13.17* | 10.68 | | 0.128 | 0.148 | 8.58 | 7.67 | 7.93 | 5.80 | 5.93 | 4.09 |
| Sit-to-Walk | 0.690 | 0.757 | | 6.60 | 3.89 | 12.12 | 0.130 | 0.106 | | 19.51** | 17.52** | 15.72* | 15.97 * | 22.51*** | 29.30*** |
| | 0.690 | | 0.732 | 58.98*** | 22.07** | 23.40*** | 0.130 | | 0.120 | 41.46*** | 22.75*** | 21.70** | 63.67 *** | 33.62*** | 24.19*** |
| | | 0.757 | 0.732 | 40.47*** | 38.20*** | 54.92*** | | 0.106 | 0.120 | 27.57*** | 28.74*** | 27.08*** | 45.53 *** | 54.96*** | 60.52*** |

*P < .05, **P < .01, ***P < .001.

[a] Data are 95% prediction ellipsoid extensions and chi-square ($\chi^2$) indices for inter-group comparisons.

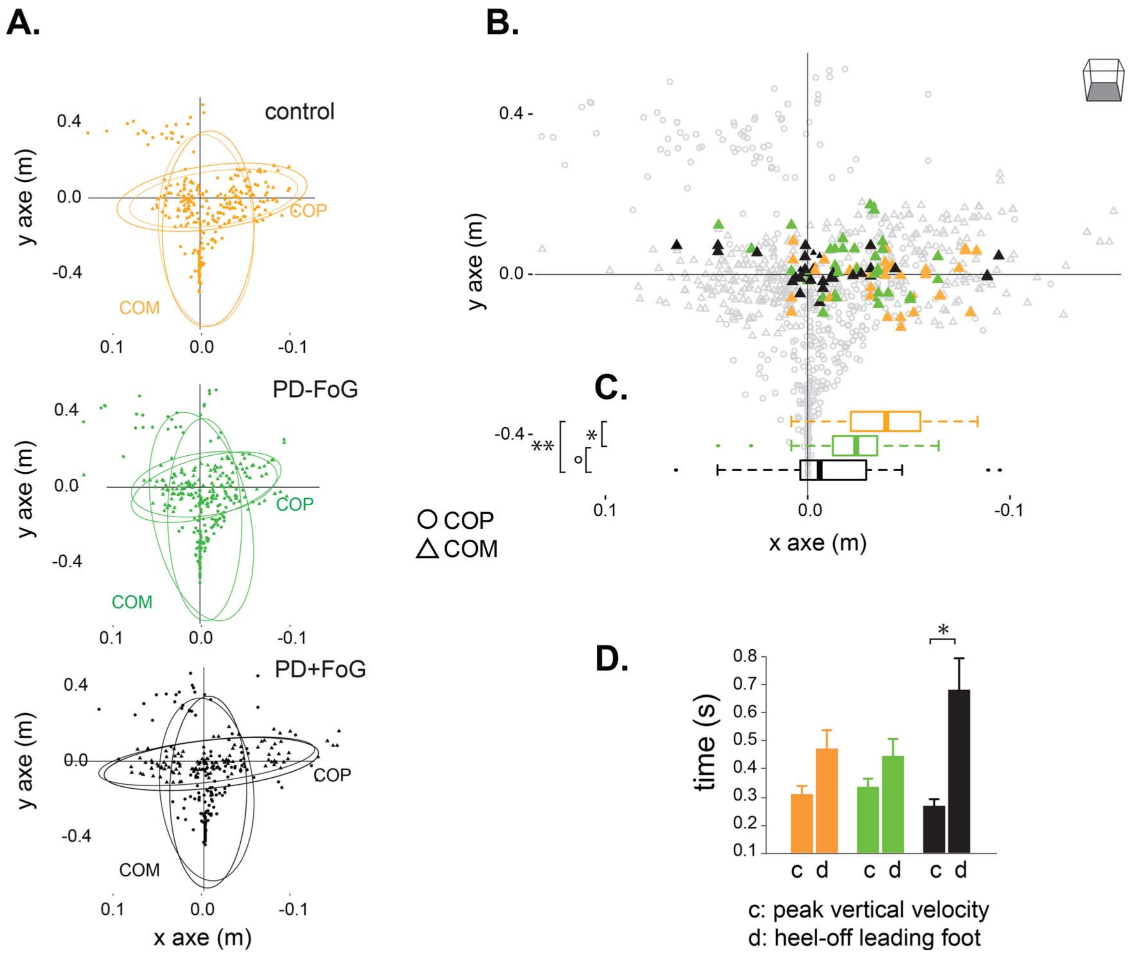


**Fig. 2.** [A] illustrates different COP & COM positions on axial plane separated for the three groups of participants during sit-to-walk (STW) with and without concomitant cognitive task. The extent of spatial variability is graphically represented trough 95% prediction ellipses. [B] focus attention on COP positions recorded during the unloading phase (T3) of STW-task (single task condition). [C] boxplot of COP positions at heel-off leading foot (Wilcoxon-Mann-Whitney *Z*: ** p = 0.005; * = 0.03; ° = 0.077) (single task condition). [D] Comparison of the extension phase at the peak vertical velocity (c), and the unloading phase at the heel-off (d) during the STW task (single task condition), within the three groups of participants (Friedman $\chi^2_1$: * = 0.02).

probability contour (i.e., standard ellipsoid) of the measured data. Between groups inferential tests were conducted on GVs with a Chi-square log-Likelihood Ratio Test [30,31]. Given that this procedure is very sensitive to outliers we approached the problem using a classical Minimum Volume Ellipsoid (MVE) algorithm for detection of multidimensional outlier [32], and conducting groups comparison on selected robust subsets besides raw data. All statistical analyses were programmed using R [33] with the MASS and rrcov packages [34,35].

## 4. Results

The comparison of demographic and clinical data between participants is presented in Table 1. Clinical examination showed no altered foot characteristics (motor and sensory) in our sample. During the three tasks, we verified for the presence of a correct step progression (taligrade, plantigrade and digitigrade stance) on both feet. Moreover, we found no differences in the comparison of the execution time for each task and group (Table 2).

Fig. 1 shows average rate of correct discriminations between groups produced by LDA algorithm trained over the three tasks. Overall, the LDA trained with the first 4 Principal Components (PC) shows that STW is the task that produce the higher discrimination rates among the groups. Of the three tasks STW produced the best discrimination results between PD + FoG versus PD-FoG, and PD-FOG versus control (healthy participants). In the comparison PD + FOG versus control, both STW and Walk task discriminate better then GI.

Table 3 gives a measure of ellipsoids major axe extension (see Fig. 2A) and Chi-square log-Likelihood Ratio Test indices relative to intergroup comparisons for all tasks (COP and COM data). Generally, STW task produced significant Chi–squares for all pairwise comparisons. Particularly, between-groups discriminability seems to be nested into COP rather than COM data (see also Fig. 2A – horizontal ellipses). Moreover, these results are not driven by potential multivariate outliers since they replicate in “good” subset determined by the MVE algorithm for robust covariance estimation. The same pattern of data was observed with the concomitant cognitive task, (data not shown on tables). The relevance of COP component in STW task (without concomitant cognitive task) to maintain postural control is evident in the transition phase from “sit-to-stand” to “stand-to-walk” (Fig. 2B and Fig. 3 – top left plate): COP positions recorded over the three groups at leading foot heel-off moment was significantly different (Kruskal-Wallis $\chi^2_2$ = 10.260; p = .006), with PD + FoG group that had delayed shifting of weight towards the leading foot more than PD-FoG and Control groups respectively, both spatially (Fig. 2C and Fig. 3 – top left plate) and temporally (Friedman $\chi^2_1$ = 5.261; p = .02; Fig. 2D and Fig. 3 – top left plate).

## 5. Discussion

The main result of this experimental work is that “sit-to-walk” is the motor task that best discriminate between patients with and without freezing of gait, and healthy participants. This task requires demanding

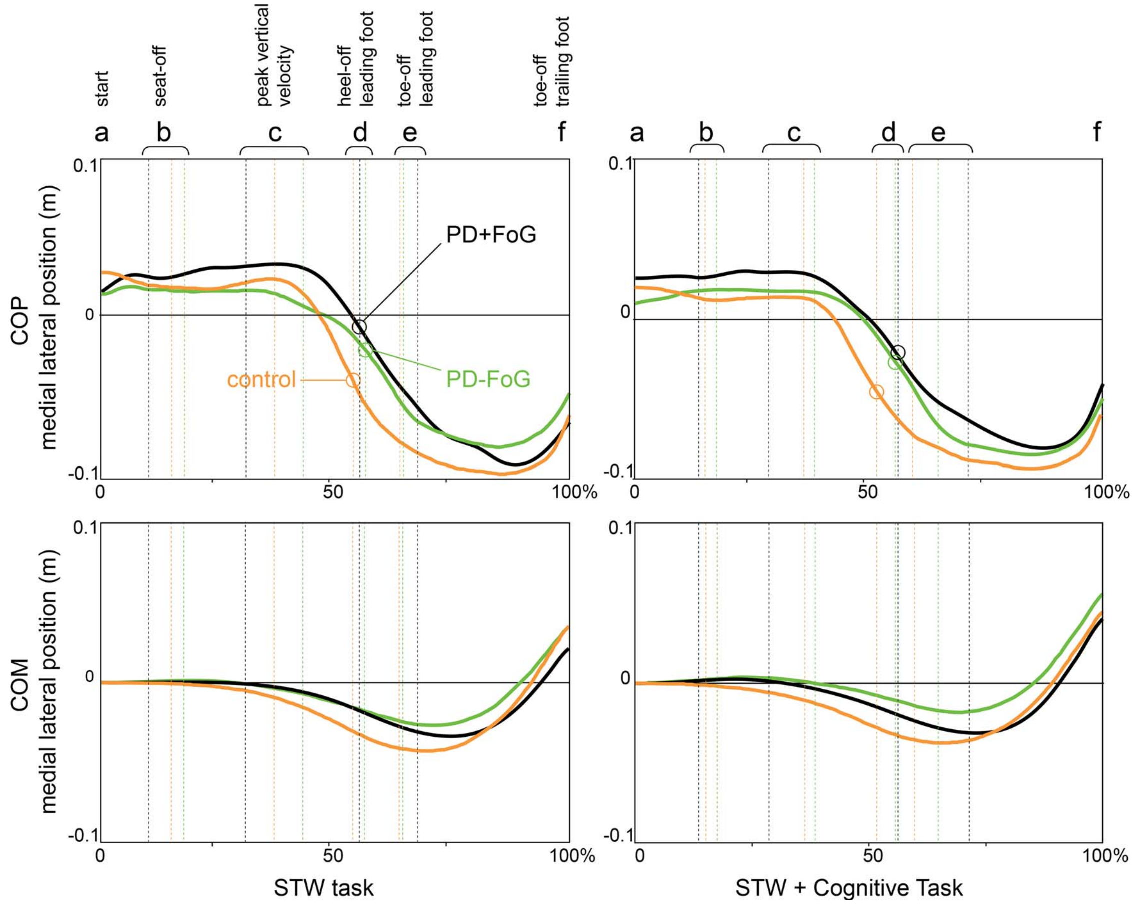


**Fig. 3.** Illustrates mean profiles of the COP and COM medial lateral positions for the Sit-to-Walk task with or without concomitant cognitive task, for the three groups of participants. The execution time has been normalized to 100%.

postural control abilities and the observed differences among groups in the spatial distribution of the COM and COP trajectories are probably due to different abilities to maintain postural balance during the movement. These differences are less evident in the GI task and absent in the W task (see Table 3), probably because it is easier to modulate active postural control in these two tasks than in STW.

Surprisingly, the adding of a concomitant cognitive task to the motor one produced no appreciable effects to movement's execution in all groups. This result was unexpected since other similar studies with PD patients report clear differences between single- and double-task execution [19]. An explanation of the cognitive task poor efficacy, could be the easiness, and, in some way, the automaticity of its execution. Moreover, the double-task condition was performed always after the single one, resulting in an easier performance. In addition, the pace of inverse naming could have been used by the patients to control their movement temporal parameters. For all these reasons, cautiously, we will base the discussion of our findings on the results of the single-task condition.

In the STW task, the comparison of the shape and spatial distribution of COP and COM trajectories on the transverse plane (Fig. 2A, Table 3) reveals that in patients without freezing the distribution of COP is circumscribed to a smaller area respect to healthy participants. Instead, trajectories of patients with freezing spread over medial-lateral space more than in the two other groups. In PD-FoG the reduction in trajectory area is probably due to a greater muscle co-activation or joint stiffness as a compensative postural strategy to maintain balance during difficult conditions. Indeed, a recent research [36] suggested that in institutionalized very old adults a lower variability in a postural strategy may improve balance ability. PD + FoG may not to have this compensatory balance control [37], showing instead larger limbs displacements produced by a deficit in postural regulation.

A qualitative analysis of the STW task, reveals that the distribution of COP positions (Fig. 3) along the medial lateral direction of patients with freezing is shifted toward the leading (left) leg during the flexion and extension phases. A similar trend, though less evident, appears in patients without freezing and in healthy participants. In addition, the timing of the seat-off and peak vertical velocity moments appear anticipated in patients with freezing, if compared with those of the patients without freezing and healthy participants. In the unloading phase at the heel-off of the leading foot – that arrive on the same time for all participants – the COP position of patients with freezing is central, instead it is shifted toward the trailing (right) leg in patients without freezing, and even more toward right in healthy participants. This last difference of position is confirmed by a direct comparison at the heel-off of the leading foot (Fig. 2C). The difference in the timing of peak vertical velocity and heel-off of the leading foot in patients with freezing respect to the other participants, which is supported by direct comparison (Fig. 2D), underlie a motor strategy characterized by a rapid flexion and extension phase followed by a prolonged slow-down in the unloading phase, showing the inability to smoothly and quickly merge the sequential motor component task of sit-to-stand and stand-to-walk. These differences in temporal and spatial displacement of COP might be attributed to a deficit in postural control, suggesting that the latter is more severe in patients with freezing.

The STW task, requiring a different motor planning, allows a better discriminability of specific postural behaviours in patients with freezing, which are not recognizable through the postural task requested in clinical tests. We hypothesized that only complex sequences in a dynamic motor task may be useful to identify postural differences between patients with and without freezing.

The limitation of the study in the choice and administration of the concomitant cognitive task reduced the possibility to find differences even more stronger between the group PD patients with FoG and the other two.

The Linear Discriminant Analysis confirms that STW is the task that better discriminated between the three groups (Fig. 1). This result is particularly important because corroborates our interpretation without using carefully pre-selected indices, but using all the data. Our study suggests that PD patients with FoG exhibit limited resources to plan demanding motor pattern, such as STW.

## Conflict of interest statement

We declare that all authors have read, and contributed to the writing of the manuscript, and no ghost writing, by anyone not named on the author list, is included. The paper has not been previously published, and it is not under simultaneous consideration by another journal.

All authors have seen and approved the manuscript in the form submitted to the journal. We declare that the manuscript is conformed to the highest standards of ethical conduct in the submission of accurate data and we acknowledge the work of others when applicable.

We declare that there are no conflicts of interest regarding this manuscript, and that we have not received any funding for this study.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version.

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