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Research Article

Freezing of gait and quiet standing: Sensory and medication influences in Parkinson's disease

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HIGHLIGHTS
- FoG and nFoG show similar postural control.
- CoP analysis outperforms ES in assessing postural control.
- Dopaminergic meds amplify sensory integration deficits in PD.
- Challenging sensory conditions reveal instability in PD.

ABBREVIATIONS

AP	Anteroposterior
BMI	Body Mass Index
CoP	Center of Pressure
df	Degrees of Freedom
ES	Equilibrium Score
FoG	Freezing of Gait
H&Y	Hoehn & Yahr
Mini-BESTest	Mini Balance Evaluation System Test
ML	Mediolateral
MoCA	Montreal Cognitive Assessment
nFoGq	New Freezing of Gait Questionaire
P	Pearson P statistical function
PCA	Principal Component Analysis
PD	Parkinson's Disease
PSD	Power Spectral Density
REML	Restricted Maximum Likelihood Estimation
RMS	Root Mean Square
UPDRS	Unified Parkinson's Disease Rating Scale

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BACKGROUND: Freezing of Gait (FoG) is a debilitating symptom of Parkinson's disease (PD), significantly impacting postural control and increasing fall risk. Traditional methods for assessing postural control, such as the equilibrium score (ES), face criticism for inaccuracies due to their limited sensitivity and reliance on fixed assumptions.
AIM: This study aimed to evaluate the influence of FoG status on postural control using center of pressure (CoP) analysis under various sensory conditions and medication states.
METHODS: The study analyzed data from 32 individuals with idiopathic PD (14 with FoG - freezers) using a force platform to measure CoP variables during quiet standing. Participants were assessed under four sensory conditions: rigid surface with eyes open, rigid surface with eyes closed, malleable surface with eyes open, and malleable surface with eyes closed. Measurements were taken in both medication ON and OFF states. Statistical analysis was performed using linear mixed-effects models.
RESULTS: Significant differences were observed in the malleable surface with eyes closed (CoP velocity and frequency in the anteroposterior direction) when participants were in ON state.
INTERPRETATION: This finding underscores the importance of investigating how dopaminergic medication affects sensory processing in individuals with FoG, as the effects of medication on postural control may vary depending on task demands and sensory conditions. The findings underscore the need to consider sensory conditions and medication status in clinical assessments and interventions to improve management strategies for postural instability and FoG in PD.

KEYWORDS: Movement disorders | Levodopa | Biomechanics | Posturography | Sensory reweighing

INTRODUCTION

Freezing of gait (FoG) is a debilitating symptom often observed in individuals with Parkinson's disease (PD). It is characterized by sudden, brief episodes of an inability to move the feet forward despite the intention to walk [1]. This phenomenon significantly impacts the quality of life, increasing the risk of falls and reducing mobility and independence [2]. The underlying mechanisms of FoG are complex and multifaceted, involving deficits in motor, cognitive, and postural control. Among these, impairments in postural stability have emerged as a key contributing factor. In this context, individuals with FoG (freezers) exhibit more instability in specific domains of postural control [3,4] than individuals without FoG (nonfreezers).

In a review, Bekkers et al. (2018) showed that 4 out of 7 studies investigating quiet standing with eyes open found no differences between freezers and nonfreezers [5–8]. These studies employed both center of pressure (CoP) metrics—such as sway amplitude, velocity, and path length—and equilibrium scores (ES). Four studies [5,7–9] analyzed the quiet posture in different sensory conditions, but the findings were contradictory regarding the effects of sensory manipulations. While some studies reported that freezers showed greater postural instability when visual or somatosensory input was disturbed, others found no significant group differences or observed different balance strategies between freezers and nonfreezers. Overall, there is a different reweighting of sensory input between groups. The results on manipulating visual information were inconsistent. Some studies reported that freezers exhibited greater postural sway or increased CoP trajectory radius when vision was removed, suggesting a higher visual dependence [7]. In contrast, other studies found no significant differences in postural control between freezers and nonfreezers under visual restriction [8,9]. Only one study analyzed quiet standing by manipulating medication and visual and somatosensory sensory information [9]. Ehgoetz Martens et al. found that sensory input during quiet standing affects postural control differently between freezers and nonfreezers. Worse postural control, greater sway amplitude and velocity of the CoP, was found in freezers compared to nonfreezers during the ON medication state when somatosensory and visual information was manipulated. The authors hypothesized that dopaminergic medication seems to specifically amplify sensory integration deficits in freezers, contributing to greater instability in their ON medication state.

However, postural control assessment was through the equilibrium score (ES) in most of these studies [5,8,9]. The ES is calculated based on the stability limit. The ES is calculated based on the maximum anterior-posterior sway angle of the center of gravity during quiet standing. It expresses the participant's sway as a percentage of a predefined theoretical stability limit. A lower ES indicates greater sway and thus poorer postural stability. This stability limit is set at 12.5º, regardless of the participant, and is based on an individual without a neurological condition. Nonetheless, there are concerns about the ES calculation: (1) Stability limits can vary significantly for some individuals, meaning the sway limit could be greater or smaller than 12.5. Thus, assumptions about the global magnitude of stability limits may introduce errors in the ES calculation for individuals with PD [10]. For example, Schlenstedt et al. (2016)[11] showed that freezers' stability limits were significantly reduced. (2) There is an asymmetry in the stability limit that is disregarded in the ES calculation. (3) Many combinations of anterior and posterior stability limits can produce the same ES. Therefore, results involving quiet stance in freezers using ES may be questioned. Considering that the most commonly used posturographic measure in postural control assessment is the center of pressure (CoP), it would be important to analyze postural control while quietly standing in freezers using CoP. Although CoP analysis is widely used in posturographic assessments of individuals with PD, studies specifically comparing freezers and nonfreezers under systematically varied sensory and medication conditions using detailed CoP metrics remain scarce. Most prior work has focused either on ES or on limited CoP parameters, often under a single sensory context. Therefore, our study aims to fill this gap by comprehensively analyzing postural control through multiple CoP-derived variables in both ON and OFF medication states and across distinct sensory conditions, thereby providing a more nuanced understanding of the postural control mechanisms underlying FoG. Therefore, this study aimed to evaluate the influence of FoG status on postural control during upright posture in different sensory conditions and quiet dopaminergic medication status in individuals with PD. We hypothesize that there will be no differences in postural control during quiet standing between freezers and nonfreezers under baseline sensory conditions, consistent with previous findings suggesting that freezing of gait and postural instability may represent independent mechanisms [3]. Additionally, we hypothesize that freezers will exhibit greater postural instability in the ON medication state when somatosensory and visual information is manipulated, based on evidence that dopaminergic medication may exacerbate sensory integration deficits in this population [9].

METHODS

Participants

We analyzed data from a data set [12] of 32 individuals with idiopathic PD (age ranged from 44 to 81 years, body mass from 53.3 to 95.6 kg, height from 151.5 to 184.0 cm, body mass index (BMI) from 17.5 to 31.5 kg/m2, Hoehn & Yahr scale between 1 to 4 and 14 freezers). Inclusion criteria were the absence of neurological or physical dysfunctions other than those associated with PD and no self-reported vestibular, visual, or somatosensory dysfunction. Participants were excluded from this study if they met one or more exclusion criteria: inability to follow the study schedule or attend scheduled visits; impossibility of understanding or carrying out the task.

Experimental procedure

Participants conducted clinical and postural control assessments in two experimental sessions, one in the ON condition of the medication and the other in the OFF condition. To be considered ON condition, participants had taken dopaminergic medication one hour before starting the session to ensure dose stabilization. In the OFF condition, the participants were at least 12 hours without using any medication for PD. The order of the sessions was randomized among the patients.

At the beginning of each condition, two experienced researchers in movement disorders applied the following scales: motor score Unified Parkinson's disease rating (UPDRS-III), Hoehn & Yahr (H&Y), New Freezing of Gait Questionaire (nFoGq), Montreal Cognitive Assessment (MoCA), and Mini Balance Evaluation System Test (Mini-BESTest). The researchers' assessments of each scale item were given by consensus. FoG was confirmed by score 1 of item 1 of the nFoGq.

Postural control was assessed by maintaining a quiet upright posture for 30 seconds on a force platform (AMTI OR6-6) in

different sensory conditions: (a) Full sensory information: standing directly on the rigid surface of the platform while keeping the eyes open. (b) Visual restriction: standing directly on the rigid surface of the platform while keeping your eyes closed. (c) Tactile restraint: standing on a foam base (on the platform), keeping the eyes open. (d) Visual and tactile restrictions: standing on a foam base (on the platform) with eyes closed.

The tasks were performed with the participants barefoot and their heels spaced 10 cm apart. For trials performed with visual information, participants were instructed to fix their gaze on a fixed point (circle 5 cm in diameter) presented on a television monitor approximately 4 m away in front and approximately at the height of the participants' eyes. For trials without vision, participants had both eyes completely blindfolded and adopted the same body position and head orientation as if they had to look at the target. For tactile restraint trials, participants stood on a 6 cm high foam base (Balance Pad, Airex AG). The force platform acquisition frequency was 100 Hz. Three attempts were performed for each experimental condition.

Data analysis

Raw force platform data were processed using MATLAB R2021a (The MathWorks Inc., Natick, MA, USA). After visual inspection, the data were filtered by a fourth-order Butterworth low-pass filter with a cutoff frequency of 10 Hz. The center of pressure (CoP) data in the anteroposterior and mediolateral directions were analyzed in the following variables:

a. CoP area: The 95% confidence ellipse area was computed using principal component analysis (PCA) to estimate the dispersion of the CoP trajectory in the anteroposterior (AP) and mediolateral (ML) directions.

b. CoP ellipse orientation: The angle of the major axis of the ellipse (in degrees) was derived from the first principal component of the CoP data.

c. Root mean square (RMS): The RMS of CoP displacement was computed separately for AP and ML directions to reflect the variability of sway.

d. Mean CoP velocity: Total CoP path length (sum of point-to-point displacement across the trial) was divided by trial duration (30 s) in both directions.

e. CoP frequency: Power spectral density (PSD) of the CoP signal was estimated using Welch's method. The frequency containing 80% of the cumulative spectral power (dominant frequency band) was extracted for both AP and ML directions.

Statistical analysis

Clinical scales were analyzed using the Wilcoxon test for intra-group comparisons (effect of medication). For kinetic data, an analysis of the homogeneity of variances and normality in the distribution of data and residuals was performed using the Levene and Shapiro-Wilk tests, respectively. In non-normal data cases, the data normalization method was selected based on the Pearson P statistical function divided by the degrees of freedom (P/df). This ratio can be compared between the different forms of normalization and indicate which of the data follows the distribution closest to normal (ratio close to 1). With the data normalized, linear mixed-effects models were fitted, using Restricted Maximum Likelihood Estimation (REML), to investigate whether CoP measures differ between groups (freezers and nonfreezers) and medication (ON and OFF). REML estimation was used to avoid bias due to sample size. Participants were considered random intercepts to account for repeated measurements within each participant. The significance level for all analyses was set at $\alpha = 0.05$. The studies were carried out using the R program (version 4.1.1).

RESULTS

Table 1 presents the clinical characteristics of individuals with PD. The two groups' UPDRS-III scores of the ON and OFF conditions differed significantly.

There was no significant difference for groups and medication in the rigid surface and eyes open conditions (all p-values > 0.13; Figure 1).

For the rigid surface and eyes closed condition (Figure 2), there was a significant difference in medication for the RMS of the CoP in the mediolateral direction ($F_{1,30} = 6.48$, $p = 0.016$, $\eta 2 = 0.09$), with higher values in the OFF medication (1.63 mm ± 1.07) in relation to ON medication (1.16 mm ± 0.61), irrespective of group.

There was no significant difference between groups and medications in the malleable surface and eyes-open conditions (all $p > 0.14$; Figure 3).

For the malleable surface and eyes closed condition (Figure 4), there was a significant difference in medication for the variables CoP velocity in the anteroposterior direction ($F_{1,30} = 5.31$, $p = 0.028$, $\eta 2 = 0.03$) and frequency of CoP in the anteroposterior direction ($F_{1,30} = 4.40$, $p = 0.045$, $\eta 2 = 0.03$). These differences were due to higher values in the OFF medication (speed: 34.48 mm/s ± 14.40; frequency: 0.67 Hz ± 0.20) compared to ON medication (speed: 29.98 mm/s). s ± 11.42; frequency: 0.61 Hz ± 0.17).

Table 1. Mean (standard deviation) of the characteristics of individuals separated by group and medication condition.

	Freezers	Nonfreezers	p-value

	ON	OFF	p-value	ON	OFF	p-value	freezers x nonfreeezers	
							ON	OFF
Age (years)	62.38 ± 12.25	-	-	67.63 ± 8.69	-	-	0.212	-
Disease duration (years)	8.15 ± 4.52	-	-	6.95 ± 4.65	-	-	0.334	-
L-Dopa equivalent (mg•day^{-1})	813.00 ± 512.47	-	-	611.95 ± 287.39	-	-	0.489	-
MoCA (score)	25.31 ± 2.75	24.77 ± 2.98	0.308	22.21 ± 4.08	22.58 ± 4.11	0.460	0.014 *	0.159
UPDRS-III (score)	16.92 ± 10.39	27.85 ± 14.85	0.002 *	18.89 ± 7.43	25.53 ± 7.95	0.002 *	0.347	0.715
Mini-BESTest (score)	26.54 ± 5.94	24.62 ± 6.01	0.056	26.42 ± 3.74	25.32 ± 4.59	0.079	0.407	0.985

MoCA: Montreal Cognitive Assessment; UPDRS-III: motor score Unified Parkinson's disease rating; Mini-BESTest: Mini-Test of Balance Assessment System scale.

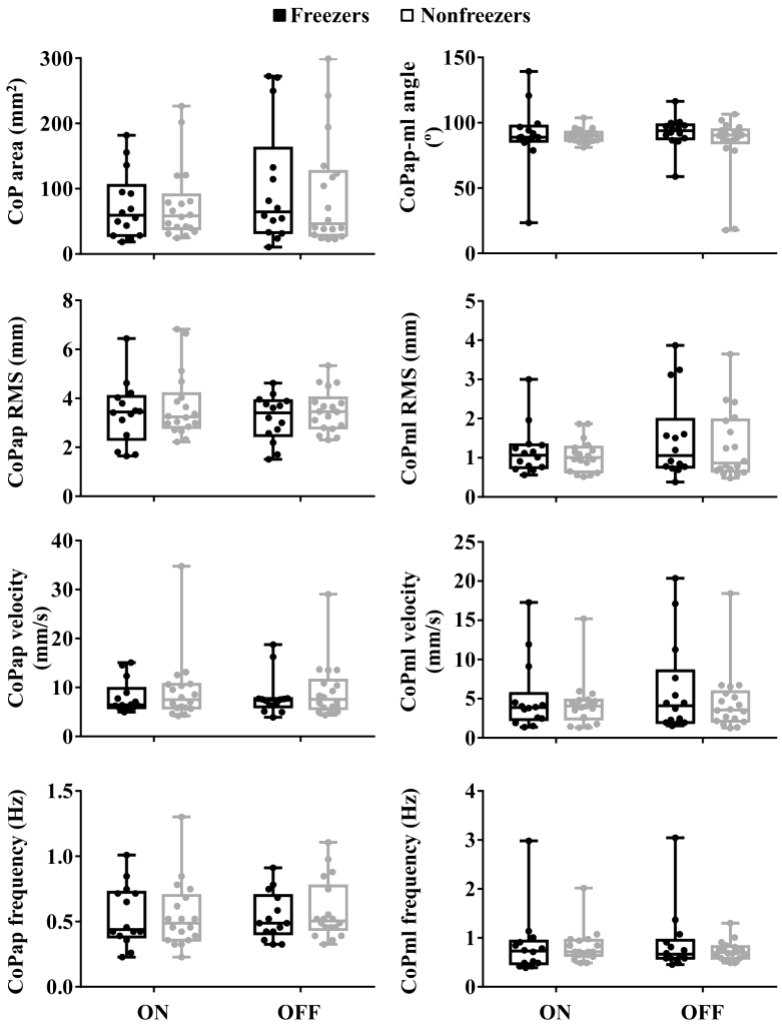

Figure 1. Boxplot (circles representing individual values) of the center of pressure (CoP) oscillation variables comparing the groups (FoG and nFoG) and medication (ON and OFF) in the rigid surface and eyes open.

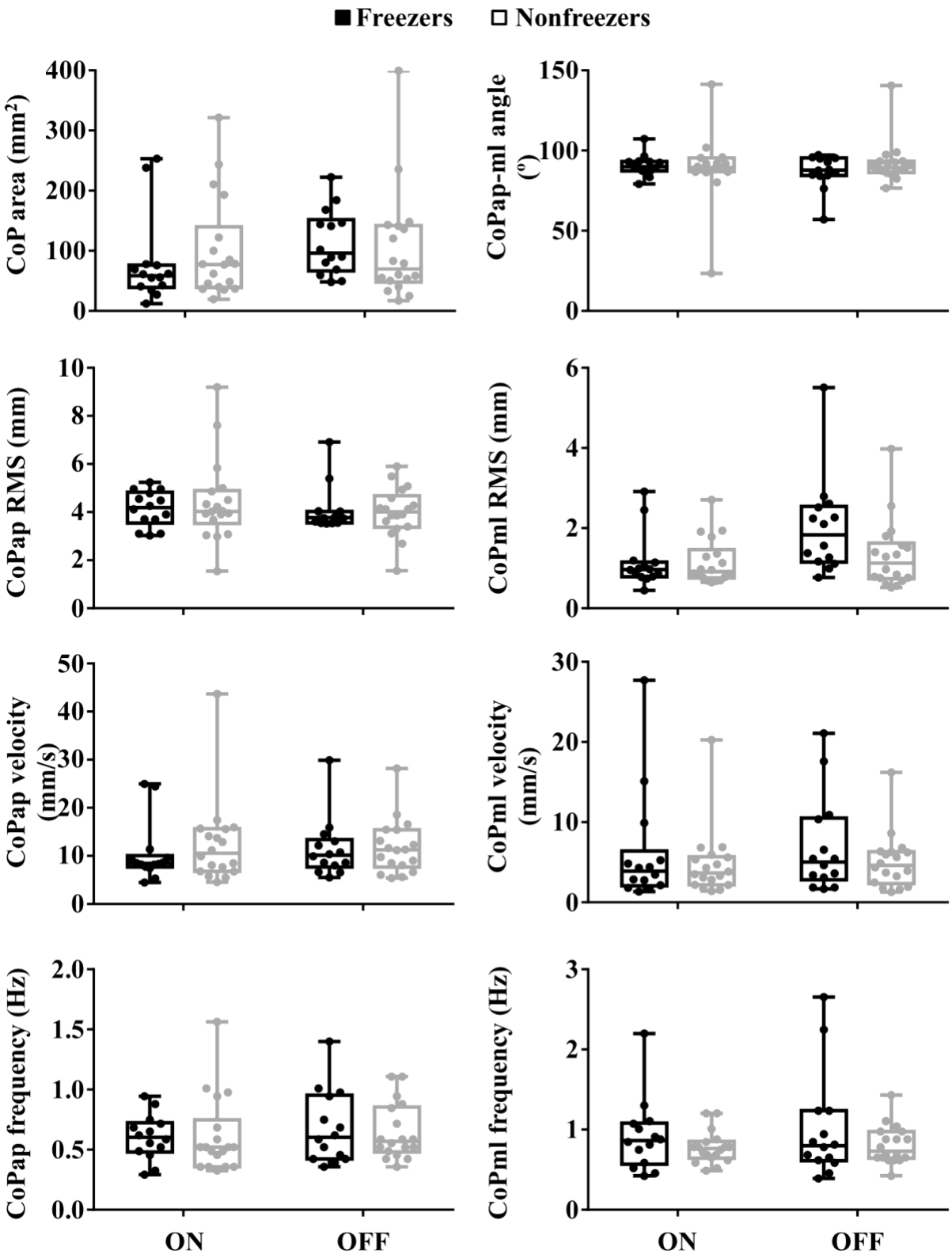

Figure 2. Boxplot (circles representing individual values) of the center of pressure (CoP) oscillation variables comparing the groups (FoG and nFoG) and medication (ON and OFF) in the rigid surface and eyes closed.

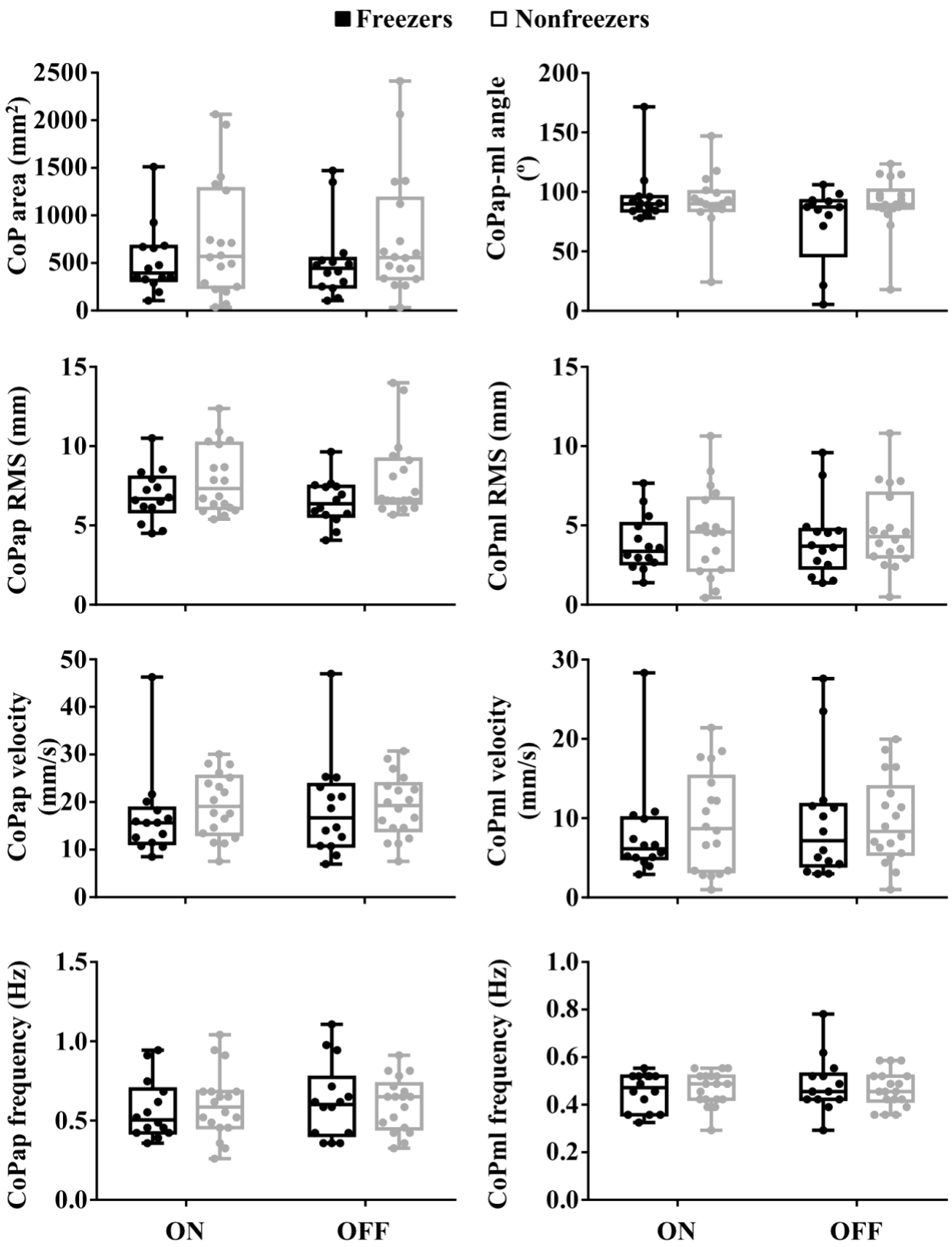

Figure 3. Boxplot (circles representing individual values) of the center of pressure (CoP) oscillation variables comparing the groups (FoG and nFoG) and medication (ON and OFF) in the malleable surface and eyes open.

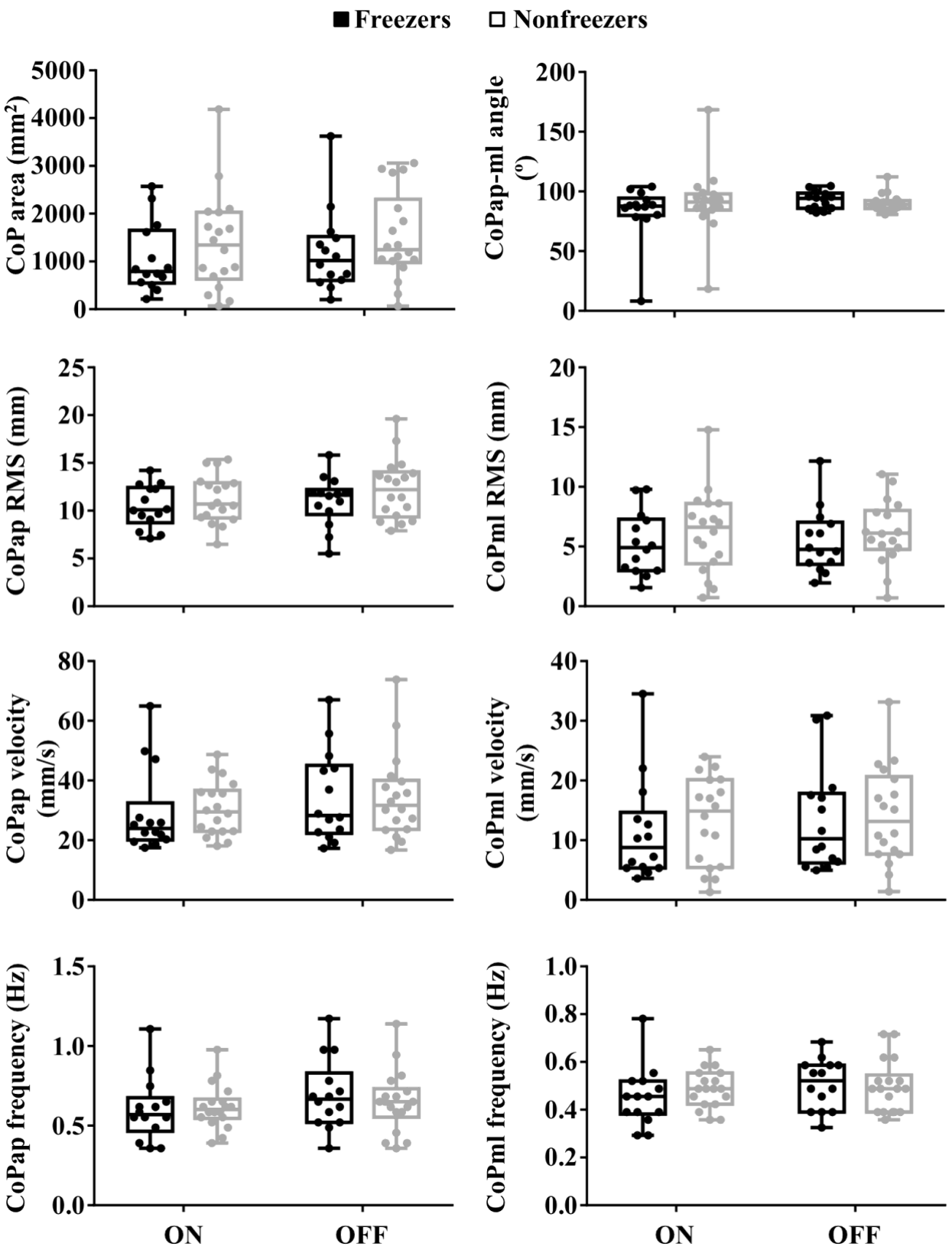

Figure 4. Boxplot (circles representing individual values) of the center of pressure (CoP) oscillation variables comparing the groups (FoG and nFoG) and medication (ON and OFF) in the malleable surface and eyes closed.

DISCUSSION

The study aimed to evaluate the influence of FoG status on postural control during quiet standing in individuals with PD under varying sensory conditions and medication states. Our results showed no significant differences in postural control between freezers and nonfreezers. However, in the malleable surface condition with eyes closed, significant group differences emerged in the ON medication state, with freezers showing increased CoP area and higher CoP velocity in the mediolateral direction compared to nonfreezers. These findings suggest that dopaminergic medication may exacerbate sensory integration deficits in individuals with FoG under conditions of reduced somatosensory and visual input.

Our results showed no significant differences in postural control during quiet standing between freezers and nonfreezers, supporting the notion that postural instability and FoG might operate independently under these conditions. Our results align with studies that relate domains of postural control with the presence and severity of FoG [13,14]. Coelho et al. [13], for instance, reported that higher FoG questionnaire (FoG-Q) scores were significantly correlated with increased CoP velocity and sway area during quiet standing, particularly under eyes-closed conditions. These findings reinforce the notion that individuals with more severe FoG exhibit greater postural instability, especially when sensory input is reduced — a pattern also observed in our study under malleable surface and eyes-closed conditions. These studies also showed that quiet standing was not related to FoG. The independent model proposed by Bekkers et al. [3] posits that postural instability and FoG are separate phenomena with distinct underlying mechanisms. Our finding of no significant differences in postural control during quiet standing aligns with this model, suggesting that under stable conditions, postural control mechanisms operate similarly in both freezers and nonfreezers. This model aligns with the idea that while FoG might manifest during dynamic movements and gait, postural instability during static conditions may not be directly influenced by the mechanisms driving FoG. Thus, the independent model highlights the importance of context-specific assessments in PD, where the interplay between sensory integration and motor control can differentially impact postural stability and FoG, necessitating distinct therapeutic approaches for each symptom.

Our results underscore the nuanced impact of dopaminergic medication on postural control in PD, particularly under challenging sensory conditions. On a malleable surface with eyes closed, individuals in the OFF-medication state exhibited significantly higher CoP velocity and frequency, indicating greater postural instability in the absence of dopaminergic input. These findings suggest that dopaminergic medication may contribute to improved postural control under reduced sensory input, particularly in certain conditions. While Levodopa is well-documented for its positive effects on alleviating general motor symptoms of PD [15], including tremors and bradykinesia, its influence on quiet standing is more complex. The medication appears to impair sensory integration and adversely affect postural stability, particularly under conditions of reduced sensory input [16], especially when compromised proprioceptive feedback [17], as in the malleable surface condition. This aligns with findings from Leroy et al. [18], who noted mixed effects of Levodopa on balance, showing improvement in some clinical balance tests but also increased postural control in quiet standing and altered balance strategies, such as a shift from ankle to hip strategies [19]. These changes can be detrimental, as they indicate a less stable, more conservative approach to maintaining balance, often associated with higher fall risk. Therefore, while dopaminergic medication remains crucial for managing PD motor symptoms, its impact on balance necessitates a tailored approach in clinical assessments and interventions, considering both the benefits and potential destabilizing effects under varying sensory conditions.

The study emphasizes the value of CoP analysis in evaluating postural control in individuals with PD, particularly under sensory-challenging conditions, as it may capture subtle dynamic changes that are not readily detected by global summary measures such as the equilibrium score [10]. Unlike ES, which uses a fixed stability limit and does not account for individual variations and asymmetries in postural stability, CoP analysis offers a detailed and precise assessment by measuring various parameters of postural oscillations, such as excursion area, root mean square, oscillation velocity, and frequency in both anterior-posterior and mediolateral directions. This approach provides a comprehensive understanding of postural control, capturing subtle differences under different sensory conditions and medication states, thus enabling more accurate diagnosis, monitoring, and treatment of postural instability in PD.

Our study has limitations. Although this is a widely accepted and routine method, it can be challenging to differentiate between individuals who freeze and those who do not, mainly when individuals with PD frequently exhibit cognitive impairments and may not be aware of FoG symptoms. The sample size of 32 individuals may limit the generalizability of the findings, and a larger cohort would be beneficial for confirming these results. Additionally, the assessment of postural control was conducted in a controlled laboratory environment, which may not fully capture the complexities of real-world conditions where postural instability and FoG occur. The exclusion of individuals with significant cognitive impairments or other comorbidities also influenced the outcomes, as these factors are prevalent in the PD population and can affect postural control. Furthermore, although the study focused on the impact of dopaminergic medication, it did not account for the potential effects of other medications or interventions that participants might have been using.

These laboratory-based findings have direct implications for clinical practice. Tasks involving reduced sensory input, such as quiet standing with eyes closed on a compliant surface, simulate common real-world challenges like navigating in dim lighting or on uneven terrain. Our results suggest that individuals with Parkinson's disease—particularly those with freezing of gait—may benefit from clinical assessments that include sensory-manipulated balance tasks to identify better instability not captured under baseline conditions. Furthermore, rehabilitation programs incorporating multisensory balance training and environmental adaptation strategies (e.g., contrasting floor textures, lighting cues) may enhance postural control and reduce fall risk in daily life. Clinicians may also consider the

timing of medication in relation to exposure to challenging environments, given the nuanced effects of dopaminergic therapy observed in our study.

CONCLUSION

In conclusion, this study highlights the complex interplay between FoG, postural control, and dopaminergic medication in individuals with PD. Our findings indicate that postural control during quiet standing does not significantly differ between freezers and nonfreezers, supporting that these two phenomena may operate independently under stable conditions. However, significant postural instability was observed in both groups while on dopaminergic medication, particularly under challenging sensory conditions, such as standing on a malleable surface with eyes closed. This underscores the importance of context-specific PD assessments and interventions, where sensory conditions and medication states should be carefully considered. Clinically, the results emphasize the need for more precise and detailed methods, such as CoP analysis, over traditional ES to accurately assess and monitor postural control. Such tailored approaches can enhance the management of postural instability and FoG, ultimately improving the quality of life and reducing fall risk for individuals with PD.

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