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Impaired directional perception of whole body perturbations in people with Parkinson's disease may contribute to balance impairment

Sistania M. Bong BS,[1] J. Lucas McKay PhD MSCR,[1] Stewart A. Factor DO,[2] Lena H. Ting PhD[1,3]

[1]Wallace H. Coulter Department of Biomedical Engineering, Georgia Tech and Emory University, Atlanta, GA USA
[2]Department of Neurology, Emory University School of Medicine, Atlanta, GA USA
[3]Department of Rehabilitation Medicine, Emory University, Atlanta, GA USA

Introduction

- Parkinson's Disease (PD) is recognized as a motor disorder, with postural instability as a primary cardinal sign, and falls due to loss of balance.
- Falls in PD has been strongly associated with the loss of control of center of mass [11].
- Automatic postural control is impaired in older adults and individuals with balance impairments leading to heavy reliance on attentional mechanism [2].
- Conscious and attentional perception of sensory information may be important to compensate for the deficit in automatic postural control [2,3].
- Sensory deficits in PD have been investigated in isolated limbs [5,6], and across different task [7,8,9], but it is unknown whether the perception of whole body motion during standing balance is degraded during standing balance or associated with balance impairment as seen in PD.

Our hypotheses are:

1. Directional acuity to whole body perturbations during standing is worse in people with PD compared to neurotypical older adults (NOA).
2. Impaired directional acuity is associated with worse balance ability in PD

Methods

Data sources

1. **PD subjects**
- Recruited from a one-year longitudinal observational study of fall risk
- 12hour off medication state
- Interviewed for health history, previous falls, and assessed with a behavioral and cognitive outcome measure including MDS-UPDRS III
- Inclusion criteria: diagnosis of Parkinson's disease (ICD-10 CM G20)
- Exclusion criteria: other significant musculoskeletal or neurological impairment that would interfere with balance and gait

2. **NOA subjects**
- Age and gender were matched to PD subjects.
- Same interview and assessment as in PD excluding MDS-UPDRS III
- Inclusion criteria: normal perception of vibration and light touch on feet
- Exclusion criteria: no PD diagnosis, otherwise same as above

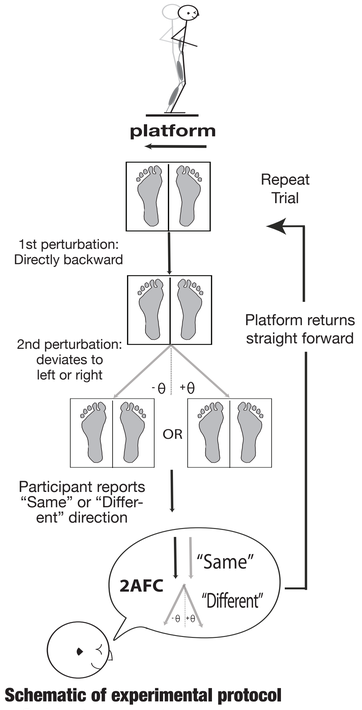
Participants

Table 1. Demographic and clinical features of study participants with PD and neurotypical older adults (NOA)

Characteristic	PD (OFF)	NOA	p-value
N	20	12	
Age, y	64.4 ± 6.7	64.2 ± 7.9	0.99
Sex			
Female	8(40)	6 (50)	
Male	12 (60)	6 (50)	
Height, cm	172 ± 11.3	173 ±10.2	0.84
Weight, kg	80.1 ± 9.5	84.0 ± 14.6	0.37
MoCA, /30	27.3 ± 2.2	27.4 ± 25	0.88
Education, y	16.3 ± 1.8	15.7 ± 1.7	0.41
Disease duration, y	8.0± 5.2		
MDS UPDRS-I, /52	11.1 ± 5.4		
MDS UPDRS-II, /52	13.3 ± 5.7[a]		
MDS UPDRS-III, /108	27.9 ± 9.8		
MDS UPDRS-IV, /24	4.8 ± 2.4[a]		
FOG-Q, /24	4.5 ± 3.9		
LEDD, mg[b]	806 ± 471		
Mini-BESTest, /28	22.2±3.3	25.7 ± 1.7	0.0018
Falls, 6 months			
0	8 (40)		
1	6 (30)		
3+	6 (30)		
Freezing of Gait			
Freezer	8 (40)		
Non-freezer	12 (60)		

Abbreviations: PD, Parkinson's disease; NOA, neurotypical older adults; MoCA, Montreal Cognitive Assessment; UPDRS-III, Unified Parkinson's Disease Rating Scale, Part III: Motor Exam; FOG-Q, Freezing of Gait Questionnaire; LEDD, Levodopa Equivalent Daily Dose. [a]N=19; one participant had not yet begun antiparkinsonian medication treatment at study enrollment.

Whole body directional acuity was measured in standing during support surface



Schematic of experimental protocol

Subject preparation:
A. Blindfold
B. Headphones playing white noise
C. Standardize stance width

Just Noticable Difference (JND) identified using Parameter estimation by sequential testing (PEST)

- Adaptive algorithm uses subject's previous responses in determining the next stimulus.
- Targets a 75% correct response threshold
- Determines the directional threshold of each side as the step size falls to 0.5°.

Data Analysis:

- Left and right thresholds were reclassified as maximum and minimum thresholds for each subject.

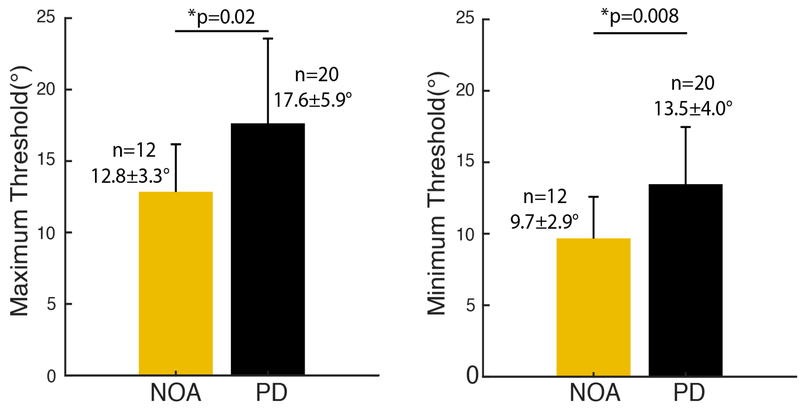
Statistical Analyses:

Statistical analyses performed in SAS at $p<0.05$.

1. Differences between maximum and minimum directional thresholds within each group was analyzed using paired t-test.
2. Differences between PD and NOA thresholds were analyzed using unpaired t-test.
3. Relationship between thresholds and MiniBESTest, MDS-UPDRS III, and disease duration were investigated using linear regression.

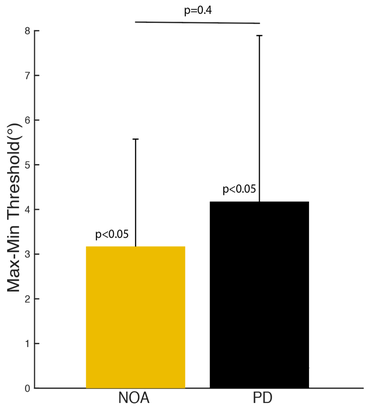
Results

1. Directional acuity is worse in individuals with PD compared to NOA



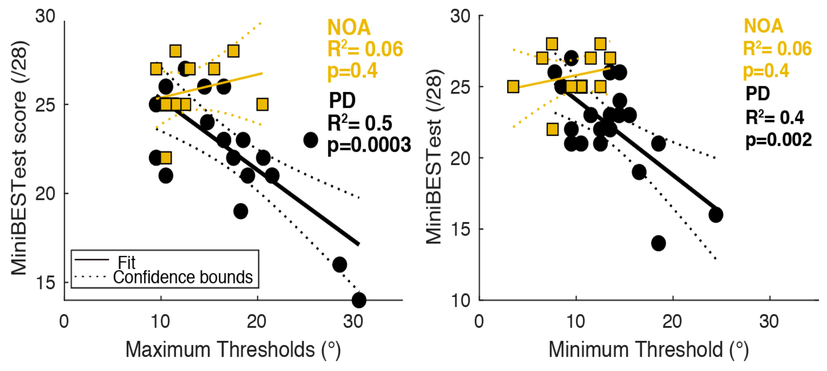
- Both the maximum (worse) and minimum (better) thresholds in PD group were siginifically greater than the maximum and minimum thresholds in NOA respectively.

2. Perception of direction was asymmetric in both PD and NOA groups



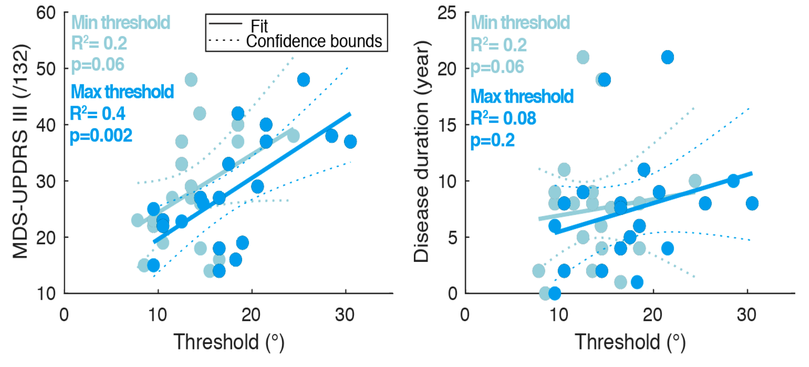
- In each group, the maximum thresholds were significantly larger from the minimum thresholds, which indicated asymmetry in perception of direction between the left and right sides.
- However, asymmetry was comparable across groups.

3. Impaired directional acuity is associated with balance impairment in PD but not in NOA



- MiniBESTest scores were inversely correlated with maximum and minimum thresholds among PD subjects, but no significant correlation between thresholds and MiniBESTest scores in NOA subjects

4. Impaired directional acuity is associated with PD symptom severity but not PD disease duration



- Among subjects with PD, the disease severity, as evaluated by MDS UPDRS-III, was positively correlated with maximum thresholds.
- Directional thresholds were not correlated with disease duration.

Discussion

- **This is the first study demonstrating that perception of whole body motion direction is impaired in people with PD in a functional context.**
- **The correlation between poor whole-body movement perception and poor balance ability suggests that perceptual impairments could contribute to balance impairments that cause falls in people with PD.**
- **The correlation between poor whole-body movement perception and disease severity observed only at the less sensitive side of perception suggests that perceptual impairments could contribute to disease severity. However, whole-body movement perception was not associated with disease duration.**
- **Perception of whole-body movement is asymmetric in individuals with or without PD.**
- **Taken together, we suggest that reduced whole-body directional perception could impair the efficacy of compensatory balance strategies that rely on attentional mechanisms, which may be necessary to compensate for poor automatic postural responses in people with PD.**

Limitations & Future Directions

- Some PD subjects with more impaired balance were unable to complete the protocol, thus we were unable to investigate the extend of perceptual impairment in more advanced PD.
- This study used univariate linear regression to assess directional acuity threshold and clinical scores. Subsequent analysis will use a multivariate regression approach to control for potential clinical and demographic factors.

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