Increased antagonist activation during reactive balance is associated with Parkinson's disease and impaired balance ability

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Introduction

Increased antagonist leg muscle activity could indicate increased muscle co-contraction and serve as a useful tool for clarifying the mechanisms of balance impairments in Parkinson's disease (PD).

Prior studies showed that people with PD demonstrate earlier, longer, and larger antagonist muscle activation in automatic postural responses (Horak 1996, Dimitrova 2004, Carpenter 2004, St George 2012).

The generalizability of these findings is limited by participants being selected for postural difficulties and minimal tremor or by small sets of muscles and perturbation directions.

Our main objective was to test whether increased antagonist activation (quantified as decreased muscle modulation) was present in a group of PD patients who were not restricted by phenotype.

Methods

Study Design:

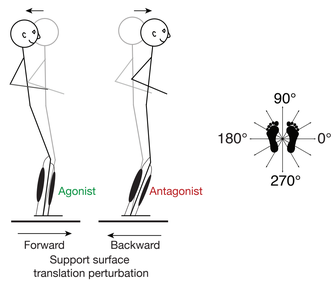
We compared antagonist activation (muscle modulation) in people with and without PD.

- Used baseline measures from a longitudinal study of exercise-based rehabilitation
- Outcome: Muscle modulation during balance responses
- Predictors: PD, age, balance ability (Fullerton Advanced Balance Scale [FAB]; Schlenstedt 2015, 2016), PD severity (Unified Parkinson's Disease Rating Scale III [UPDRS-III]; Fahn & Elton 1987), PD phenotype (Stebbins 2013)

Experimental Protocol:

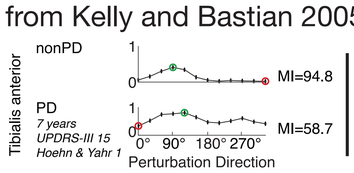
Reactive balance testing performed while OFF antiparkinsonian medication

- Surface EMG from 11 lower leg muscles during trials in which participants independently maintained balance with feet in place
- Support-surface translation perturbations in 12 directions given in a randomized order
  - 7.5 cm peak displacement, 15 cm/s peak velocity, 0.1 g peak acceleration; 28 cm stance width



Data Analysis:

Tuning curves were assembled from EMG spanning 70-450 ms after perturbation onset. Antagonist activation across perturbation directions was quantified from tuning curves with a muscle modulation index (MI) adapted from Kelly and Bastian 2005.



$$MI = 100 * \frac{\text{mean EMG}_{\text{direction of max activation}} - \text{mean EMG}_{\text{direction of min activation}}}{\text{mean EMG}_{\text{direction of max activation}}}$$

Statistical Analyses:

Univariate analyses: Associations between PD (or age>median or balance<median) and the presence of low muscle modulation (MI<median) were expressed as odds ratios (OR) for each muscle.

- OR>>1 indicate that the presence of the risk factor is highly associated with the presence of the outcome (low modulation). Chi-square tests assessed significance.

Multivariate analyses: Linear mixed models examined the relationship between modulation (MI) across all muscles and predictors PD, age, balance ability (FAB), PD severity (UPDRS-III), PD phenotype, and the interaction between PD and age.

Results

1. PD group included people with Tremor-Dominant, Postural Instability and Gait Difficulty, and Indeterminate phenotypes.

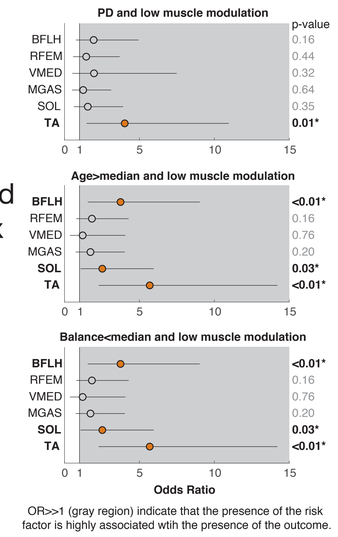
Table 1. Demographic and clinical characteristics of the study population.

	PD	nonPD	
N	31	13	
Demographic			
Female (N, %)	14, 45%	7, 54%	
Age, years, mean±SD	67.6 ± 8.8	64.5 ± 8.8	
Behavioral			
Fullerton Advanced Balance Scale (FAB, 0-40), mean±SD	29.2 ± 5.7	33.1 ± 3.1	*
Fall history in previous 12 months (N, %)			*
0 falls	13, 42%	10, 77%	
1 fall	3, 10%	2, 15%	
≥2 falls	15, 48%	1, 8%	
PD clinical features			
PD duration, years, mean±SD	7.5 ± 5.9	-	
UPDRS-III (0-108), mean±SD	31.7 ± 9.5	-	
Hoehn & Yahr Stage, (N, %)		-	
1	1, 3%	-	
1.5	5, 16%	-	
2	13, 42%	-	
2.5	4, 13%	-	
3	8, 26%	-	
PD phenotype, (N, %)		-	
Postural Instability and Gait Difficulty (PIGD)	19, 61%	-	
Tremor-Dominant (TD)	9, 29%	-	
Indeterminate (ID)	3, 10%	-	
Freezing of Gait, (N, %)		-	
Freezer	14, 45%	-	
Non-freezer	15, 48%	-	

*p<0.05

2. In univariate analyses, PD, higher age, and lower balance ability were associated with low modulation in some muscles.

- PD was associated with low modulation index in 1/6 muscles.
- Higher age was associated with low modulation index in 3/6 muscles.
- Lower balance ability was associated with low modulation index in 3/6 muscles.



OR>>1 (gray region) indicate that the presence of the risk factor is highly associated wtih the presence of the outcome.

3. In multivariate analyses, linear mixed models identified significant associations between modulation index and PD, balance ability, and PD severity but not age.

Table 2. Associations between study variables and muscle modulation index MI

	β	95% CI	P	Linear Regression
PD	-4.26	-8.31, -0.21	0.04*	$MI_{ijk} = \beta_0 + \beta_{PD} \cdot PD + \sum_{i=1}^{N_m-1} \beta_{1i} \cdot Muscle_i + \sum_{j=1}^{N_p-1} \beta_{2j} \cdot Participant_j + \epsilon_{ijk}$
Age	-0.18	-0.40, 0.03	0.10	$MI_{ijk} = \beta_0 + \beta_{Age} \cdot Age_c + \sum_{i=1}^{N_m-1} \beta_{1i} \cdot Muscle_i + \sum_{j=1}^{N_p-1} \beta_{2j} \cdot Participant_j + \epsilon_{ijk}$
FAB	0.38	0.005, 0.75	<0.05*	$MI_{ijk} = \beta_0 + \beta_{FAB} \cdot FAB + \sum_{i=1}^{N_m-1} \beta_{1i} \cdot Muscle_i + \sum_{j=1}^{N_p-1} \beta_{2j} \cdot Participant_j + \beta_{3j} \cdot Age_c + \epsilon_{ijk}$
PD Severity	-0.16	-0.26, -0.05	<0.01*	$MI_{ijk} = \beta_0 + \beta_{PD\,Severity} \cdot UPDRSIII + \sum_{i=1}^{N_m-1} \beta_{1i} \cdot Muscle_i + \sum_{j=1}^{N_p-1} \beta_{2j} \cdot Participant_j + \epsilon_{ijk}$
PD Phenotype				$MI_{ijk} = \beta_0 + \sum_{i=1}^{N_{Pheno}-1} \beta_{Pheno} \cdot Pheno + \sum_{i=1}^{N_m-1} \beta_{1i} \cdot Muscle_i + \sum_{j=1}^{N_p-1} \beta_{2j} \cdot Participant_j + \epsilon_{ijk}$
PIGD	-3.25	-7.67, 1.18	0.15	
TD	-5.22	-10.55, 0.12	0.06	
ID	-7.82	-15.69, 0.04	>0.05	
PD•Age	-0.36	-0.83, 0.10	0.13	$MI_{ijk} = \beta_0 + \beta_{PD,Age} \cdot PD \cdot Age_c + \sum_{i=1}^{N_m-1} \beta_{1i} \cdot Muscle_i + \sum_{j=1}^{N_p-1} \beta_{2j} \cdot Participant_j + \beta_{3j} \cdot PD + \beta_{4j} \cdot Age_c + \epsilon_{ijk}$

*p<0.05. Abbreviations: FAB, Fullerton Advanced Balance Scale; PIGD, Postural Instability and Gait Difficulty; TD, Tremor-Dominant; ID, Indeterminate.

Discussion

- Abnormal antagonist activity occurs across a broad sample of people with PD, muscles, and perturbation directions.
- While PD, higher age, and lower balance ability were associated with low modulation index in univariate analyses, multivariate linear mixed models accounting for effects of muscle and participant found PD diagnosis, PD severity, and balance ability - but not age - to be significant predictors of modulation.
- Increased antagonist activity may be a mechanism of balance impairment in PD, making it a potential target for rehabilitation.
- The association between muscle modulation and balance ability suggests that increased MI could serve as a marker of improved balance, even before clinical scores improve.

References & Acknowledgements

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This work was supported by NIH R21 HD075612-01, NIH TL1TR000456, UL1 TR000424, K25 HD086276, and R01 HD46922-10.

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