Assessment of Gait Abnormalities in Individuals with Parkinson's Disease With and Without Suspected Cholinergic Deficits

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INTRODUCTION

- Parkinson's disease (PD) is a neurodegenerative disorder associated with the reduction of dopamine in the basal ganglia, characterized by a clinical spectrum of motor and non-motor presentations[1].
- Differences in cholinergic system degeneration may explain some of the clinical variations seen in patients with PD[2] .
- The specific features of cholinergic degeneration seen in PD are impaired cognition, slower gait speed, falling, rapid eye movement sleep behavior disorder (RBD), and impaired olfaction[1].

PURPOSE

- The motivation of this study was to test whether or not cholinergic system degeneration, in addition to basal ganglia deficits, contributes to varying gait deficits seen with PD.
- The primary hypothesis of this study is that patients with suspected cholinergic deficits, based on simple clinical testing, will be associated with more impaired gait at the Emory Movement Disorders Clinic.

METHODS

Design
- Observational, cross-sectional study performed in a movement disorders clinic in an urban setting, recruiting sequential patients.

Study population
- Goal: to recruit 200 participants for a 10% representative sample of the Parkinson's patients seen in the Emory Movement Disorders Clinic
- Inclusion criteria for enrollment:
  - Diagnosis of idiopathic PD or other parkinsonian syndromes
  - Ability to provide informed consent in English
- Exclusion criteria for gait assessment:
  - Lower extremity weight bearing restriction
  - Lower extremity botulinum toxin in previous 3 months
  - Safety concerns with ambulation

Enrollment
- Patients were invited for participation by their physician.
- Patients who met the inclusion criteria provided informed consent before undergoing a brief clinical interview.
- Patient anthropometrics, including hip width and leg length, were taken in order to normalize gait data.

METHODS

Clinical Interview
- Participants were assessed for clinical study variables during a brief interview.
- Height, weight, fall history, amount of school completed, overall self-assessed mobility and health, joint pain, and the presence of RBD were all reported subjectively[3,4].
- A separate member of the study staff obtained further demographic information from the patient's electronic medical record.

Gait Testing
- Eligible patients underwent gait testing on a pressure-sensitive walkway.
- The gait assessment consisted of walking 25 feet along one side of the mat, turning around a cone, and walking back to the starting end of the mat.
- Each participant completed a trial turning clockwise and counterclockwise to account for the presence of lateralized symptoms.
- Patient instructions:
  - Walk at comfortable pace
  - Remain silent during testing
  - Use an assistive device if needed for safe ambulation

Figure 1. Protokinetics Zeno Gait Mat

Data Processing

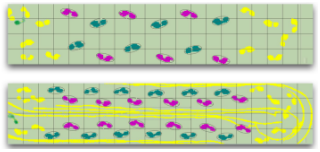


Figure 2. Processing of Gait Assessment

- Start/stop and turn were not processed in the gait analysis to eliminate bias in acceleration and deceleration.
- Gait speed (statures/s), step length (statures), and stride width (% inter ASIS) were recorded.
- The statistical analyses were performed by J. Lucas McKay, Ph.D, M.S.C.R.

LIMITATIONS

Limitations
- Inter-rater reliability may be affected due to 10+ study staff
- Gait data collected in a potentially distracting environment
- Potential misclassification bias due to the possibility of overestimating number of patients as normocholinergic, which could increase variance
- Potential underestimation of refusal rate due to communication with clinic physicians

RESULTS

Figure 3. Consort diagram of study participants

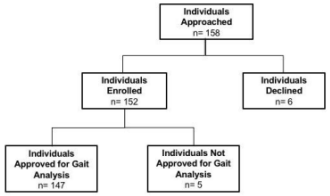


Table 1. Demographic and clinical characteristics of the study population

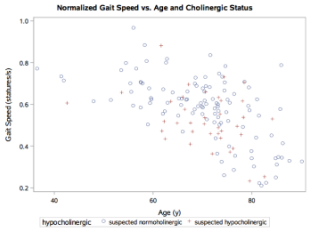
Characteristics	Value
N	152
Gender (N=59)	
Female	20 (34%)
Male	38 (64%)
Unknown/not reported	1 (2%)
Age, y (mean±SD)	70±10
Race (N=59)	
White	48 (81%)
African American	4 (7%)
Unknown/not reported	7 (12%)
Ethnicity (N=59)	
Not Hispanic or Latino	44 (75%)
Hispanic or Latino	15 (25%)
PD duration, y (mean±SD) (N=59)	7±5
Education Level	
Graduate	55 (36%)
College	49 (32%)
Junior college	12 (8%)
High school	33 (22%)
Less than high school	3 (2%)

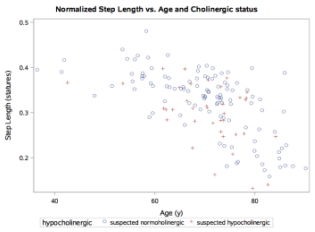
Abbreviations: PD, Parkinson's disease.

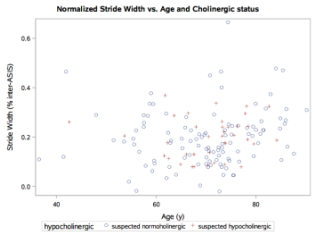
Table 2. Study variables stratified by presence of suspected cholinergic deficits. (Mean±SD)

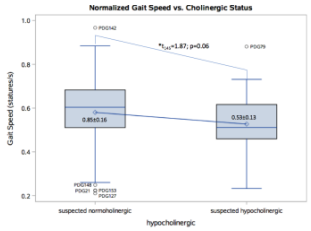
Variables	Suspected Hypocholinergic (N=37)	Suspected Normocholinergic (N=115)	Total
Gender (N=59)	N=14	N=45	
Male	7 (50%)	31 (69%)	38
Female	6 (43%)	14 (31%)	20
Unknown	1 (7%)	0 (0%)	1
UPDRS-III*(N=52)	19.2 ± 8.8	17.8 ± 11.0	
UMRBDQ C†			
Unknown/sleep alone	N/A	N/A	12
1. Never	0	75	75
2. Rarely (less than a month)	11	11	22
3. Sometimes (1-3 times a month)	8	10	18
4. Frequently (1- 6 times a week)	14	5	19
5. Almost always (Nightly)	4	2	6
RBD (N=140)	N=37	N=103	
+	37	28	65
-	0	75	75
# of falls	1.9 ± 0.9	0.6 ± 1.1	

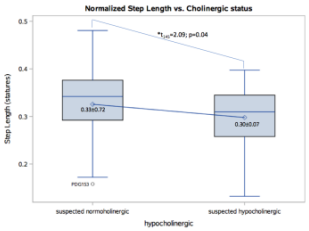
Abbreviations: *Unified Parkinson's Disease Rating Scale, †University of Michigan RBD Questionnaire

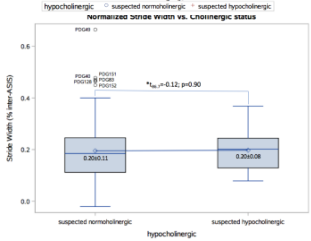












RESULTS & DISCUSSION

- Of the 147 individuals that underwent gait analysis, 37 were classified as suspected hypocholinergic and 115 were classified as suspected normocholinergic based on a brief clinical screen derived from the literature.
- After interim univariate analyses, we found that the presence of suspected cholinergic deficits was associated with an ≈11% decrease in normalized gait speed, an ≈8% decrease in normalized step length, and negligible increase in stride width.
- Clinicians can use a quick clinical screen, without interrupting facility workflow, to determine suspected cholinergic deficits.
- People with suspected cholinergic deficits have pathological changes in stance width, which may be expected in certain diseases such as AD.

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REFERENCES

1. Müller MLTM, Bohnen NI, Kotagal V, et al. Clinical markers for identifying cholinergic deficits in Parkinson's disease. *Movement Disorders*. 2015;30(2):269-273.
2. Bohnen NI FK, Studenski S, Kotagal V, Koeppe RA, Scott PJH, Albin RL, Muller MLTN. Gait Speed in Parkinson Disease Correlated with Cholinergic Degeneration. *Neurology*. 2013;81:1611-1616.
3. Consens FB, Chervin R, Koeppe RA, Little R, Liu S, Junck L, Angell K, Heumann M, Gilman S. Validation of a Polysomnographic Score for REM Sleep Behavior Disorder. *SLEEP*. 2005;28(8):993-997.
4. Chaudhuri KR, Rizos A, Trenkwalder C, et al. King's Parkinson's disease pain scale, the first scale for pain in PD: An international validation. *Mov Disord*. 2015;30(12):1625-1631.