Prevalence of neurogenic orthostatic hypotension in the idiopathic Parkinson Progression Marker Initiative cohort.

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OBJECTIVE

- To assess prevalence of neurogenic and peripheral orthostatic hypotension (nOH/pOH) in the PPMI's (https://www.ppmi-info.org) idiopathic Parkinson disease (PD) cohort, which includes patients early in their disease course
- To examine whether nOH, compared to pOH, increases likelihood or progression of depression symptoms and cognitive impairment.

BACKGROUND

- OH can occur from neurogenic causes (e.g., from neurodegeneration of autonomic structures as in PD) or from peripheral causes (e.g., volume depletion, medications, cardiac pathology).
- Several studies show an association between autonomic failure in PD, particularly presence of OH, and higher risk of cognitive decline and depression.[1,2] However, it is unresolved whether associations between OH, cognition, and depression in PD result from a hypoperfusion/cerebral ischemia-based mechanism or, alternatively, neurodegeneration of multimodal structures contributing to autonomic function, cognition, and affect.
- A recently validated calculation allows for the general categorization of OH as p/nOH based on the orthostatic ratio of heart-rate change (ΔHR) to systolic blood pressure (ΔSBP) change.[3]
- We reasoned that, should a shared neurodegenerative mechanism relate these three non-motor symptoms, then patients with nOH should be more likely to have worse cognition and depression over time than those with pOH or with no OH at all.

DESIGN/METHODS

- We downloaded PPMI data on 12/10/2020.
- We used all available data of patients coded as "PD Participant" with vital sign measurements.
- Measures of orthostatic vitals, Montreal Cognitive Assessment (MoCA), and Geriatric Depression Scale II (GDS) were extracted from screening to Visit 12.
- Patients were classified as OH+/- at each observation based on standard criteria prior to sub-classification as nOH (ΔHR/ΔSBP<0.5) or pOH (ratio>0.5).
- Prevalence of each group (OH or not) and sub-group (p/nOH) were determined at each visit.
- Crude variation in prevalence over time was determined with a χ^2 test.
- Participants with three or more observations were used to estimate associations between p/nOH at baseline and change in MoCA or GDS with time.
- Associations between presence of p/nOH and clinical/demographic variables were assessed with independent ANOVAs.

Screening Demographics

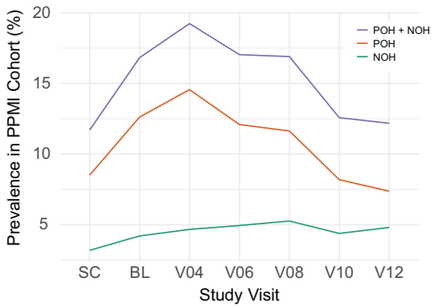
	N=472
Age	
Mean±SD	62±10
Range	34-85
Sex	
Female	298 (69%)
Male	131 (31%)
Disease duration	
Mean±SD	0.5±0.5
Range	0-3.7
MoCA	
Mean±SD	27.1±2.3
Range	17-30
GDRS	
Mean±SD	5.2±1.4
Range	1-11

RESULTS

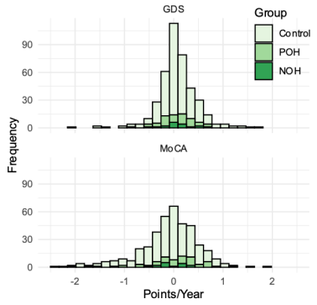
- Of N=430 idiopathic PD patients for whom orthostatic vitals were available at the baseline visit, 54 (13%) and 18 (4%) had orthostatic vitals consistent with pOH and nOH, respectively.
- Bootstrap 95% confidence intervals (BCa method) for overall pOH/nOH prevalence were 8.8–12.5% and 3.9–4.9% for pOH and nOH, respectively.

Group	Screening	Baseline	*Year 1* Visit 4	*Year 2* Visit 6	*Year 3* Visit 8	*Year 4* Visit 10	*Year 5* Visit 12	Cumulative
	N=472	*N=430*	*N=364*	*N=364*	*N=362*	*N=342*	*N=314*	*N=2648*
POH	40 (9%)	54 (13%)	53 (15%)	44 (12%)	42 (12%)	28 (8%)	23 (7%)	284 (11%)
NOH	15 (3%)	18 (4%)	17 (5%)	18 (5%)	19 (5%)	15 (4%)	15 (5%)	117 (4%)
Control	415 (88%)	356 (83%)	294 (81%)	302 (83%)	300 (83%)	299 (87%)	274 (88%)	2240 (85%)

- $\chi 2$ test of homogeneity did not reject the null hypothesis that pOH/nOH prevalence was constant (P=0.07).



- ANOVAs did not find significant variation in tested variables (age, sex, disease duration, MoCA, and GDS) with presence of nOH or pOH.



CONCLUSIONS

- In the PPMI cohort of idiopathic PD patients both neurogenic and peripheral orthostatic hypotension were likely to be present, with relatively stable prevalence over at least the first five years of disease duration. Our overall prevalence of OH in the PPMI's cohort of early PD (17%) is similar to other cohort studies examining early PD,[4] including earlier evaluation using PPMI.[1]
- We found no significant association of variation between presence of p/nOH and basic clinicodemographic variables (age, sex, disease duration), nor cognitive or depressive scale scores.
- This work is limited by its retrospective nature and use of documented orthostatic vitals; it's possible patients could have had OH from PD and 'peripheral' sources in combination. We also did not control for use of anti-hypertensives or daily levodopa equivalents
- Whether p/nOH is associated with modified presentation of other PD features in the PPMI cohort (such as activities of daily living, quality of life, motor profile), particularly compared to those without OH, and including after five years of disease duration, will be part of future investigation.

References

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