Cognitive performance and psychiatric symptoms in de novo, untreated Parkinson's disease: results from the PPMI study

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Background

- Preliminary studies suggest that cognitive impairment (**CI**) and neuropsychiatric symptoms (**NPS**) are common in newly diagnosed Parkinson's disease (PD) patients.
- Objective: To determine the frequency and correlates of CI and NPS in a large cohort of early, untreated PD patients and comparable group of healthy controls (**HCs**).

Study Design

- PPMI is an international, multi-site, case-control study conducted at 24 academic centers.
- Participants are recently diagnosed, untreated PD patients or HCs. HCs with cognitive impairment (Montreal Cognitive Assessment (MoCA) score <26 were excluded).
- Detailed cognitive and NPS battery is performed at baseline.

Linear Regression Model for MoCA Score in PD Patients

Variable	Parameter Estimate	Standard Error	Pr > F
Intercept	28.22970	0.63592	<.0001
Age	-0.45075	0.13214	0.0007
Gender	-0.45387	0.22224	0.0418
Education	0.78446	0.27501	0.0046
UPDRS Part III Score	-0.02646	0.01216	0.0301

Model used Backward Selection at 0.05 level of significance

MoCA Performance in PD

Red boxes indicate recommended cut-off score for PD-MCI (≤25) and PD dementia (≤20)

Characteristics

Variable (N [%] or mean)	PD Subjects (N =416)	Healthy Controls (N =191)	p-value (PD vs. HC)
Demographics			
Male	272 (65%)	121 (63%)	0.65
Age (Mean)	61.7	60.5	0.17
Education <13 Years	75 (18%)	28 (15%)	
Education 13-23 Years	338 (81%)	163 (85%)	0.36
Education >23 Years	3 (1%)	0 (0%)	
Not Hispanic/Latino	407 (98%)	188 (98%)	0.76
White	384 (92%)	177 (93%)	
Black/African-American	6 (1%)	9 (5%)	1.00
Asian	8 (2%)	1 (1%)	
UPDRS Mean Score & Sub Scores			
MDS-UPDRS Total Score	32.3	4.7	<0.01
MDS-UPDRS Part III (Motor)	20.9	1.2	<0.01
Hoehn & Yahr Stage			
Stage 0	0 (0%)	188 (98%)	
Stage 1	181 (44%)	2 (1%)	
Stage 2	232 (56%)	0 (0%)	<0.01
Stage 3-5	2 (0%)	0 (0%)	
Duration of Disease			
Mean (months)	6.6	NA	NA
TD/PIGD Classification			
TD	296 (71%)	NA	
PIGD	73 (18%)	NA	NA
Indeterminate	45 (11%)	NA	

Psychiatric / Non-Motor Symptoms

Variable (N [%] or mean)	PD Subjects (N = 416)	Healthy Controls (N = 191)	p-value (PD vs. HC)
GDS-15 Score			
Mean	2.3	1.3	<0.01
GDS Score			
Depressed (≥5)	58 (14%)	13 (7%)	0.01
Positive ICD Screen (QUIP+)			
Any 1 or more disorders	83 (20%)	34 (18%)	0.51
Gambling	4 (1%)	1 (1%)	0.57
Sex	12 (3%)	5 (3%)	0.84
Buying	10 (2%)	4 (2%)	0.80
Eating	35 (8%)	18 (9%)	0.70
Hobbies	29 (7%)	18 (9%)	0.31
Punding	21 (5%)	3 (2%)	0.04
Walking or Driving	3 (1%)	1 (1%)	0.77
STAI - State Score			
Mean	33.0	27.9	<0.01
STAI - Trait Score			
Mean	32.4	29.1	<0.01
UPSIT			
Mean	22.3	34.0	<0.01
Epworth Sleepiness Scale			
Sleepy (≥10)	65 (16%)	23 (12%)	0.25
REM Sleep Disorder Questionnaire			
Positive (≥5)	159 (38%)	38 (20%)	<0.01

Group	UPDRS Part I Psychosis					Fisher's exact p-value (0 vs. any positive response)
	0	1	2	3	4	
PD	402 (96.9%)	13 (3.1%)	0 (0%)	0 (0%)	0 (0%)	0.08
HC	189 (99.5%)	1 (0.5%)	0 (0%)	0 (0%)	0 (0%)	
	UPDRS Part I Apathy					
	0	1	2	3	4	
PD	348 (83.9%)	58 (14.0%)	8 (1.9%)	0 (0%)	1 (0.2%)	<0.001
HC	181 (95.3%)	8 (4.2%)	1 (0.5%)	0 (0%)	0 (0%)	

Psychiatric / Non-Motor Symptoms (Adjusted)

Variable	Odds Ratio Estimate (PD vs. HC)	Odds Ratio Confidence Limits	p-value*
GDS ≥5	2.309	(1.229, 4.348)	0.009
1 or more QUIP Disorders	1.172	(0.752, 1.828)	0.48
	Parameter Estimates (PD vs. HC)	Standard Error	p-value*
State Trait Anxiety Score			
State Anxiety Subscore	5.127	0.837	<0.001
Trait Anxiety Subscore	3.456	0.765	<0.001

*Adjusted for age (<56, 56-65, and >65) and gender

Conclusion

- Cognitive deficits based on global screening occurs in ≈20% of untreated PD patients.
- Depression, anxiety, apathy, psychosis and RBD symptoms are all more common in untreated PD compared with healthy controls.
- In contrast, ICD symptoms are not more common, supporting the probable association between ICD symptoms and dopaminergic therapy in PD.
- Results from detailed cognitive testing and cognitive categorization are pending.

**PPMI Clinical Sites

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PPMI Disclosure