

## SUPPLEMENTARY MATERIAL.

### Non-Motor Symptom Burden in Patients with Parkinson's Disease with Impulse Control Disorders and Compulsive Behaviours: Results from the COPPADIS Cohort

Jesús S, MD, PhD<sup>1,2</sup>; Labrador-Espinosa MA, MSc<sup>1,2</sup>; Adarmes AD, MD<sup>1,2</sup>; Méndez Del Barrio C, MD<sup>1,2</sup>; Martínez-Castrillo JC, MD, PhD<sup>3</sup>; Alonso-Cánovas A, MD, PhD<sup>3</sup>; Sánchez Alonso P, MD<sup>4</sup>; Novo-Ponte S, MD<sup>4</sup>; Alonso-Losada MG, MD<sup>5</sup>; López Ariztegui N, MD<sup>6</sup>; Segundo Rodríguez JC, MD<sup>6</sup>; Morales MI, MD<sup>6</sup>; Gastón I, MD<sup>7</sup>; Lacruz Bescos F, MD<sup>7</sup>; Clavero Ibarra P, MD<sup>7</sup>; Kulisevsky J, MD, PhD<sup>2,8</sup>; Pagonabarraga J, MD, PhD<sup>2, 8</sup>; Pascual-Sedano B, MD<sup>2,8,11</sup>; Martínez-Martín P, MD, PhD<sup>2,9</sup>; Santos-García D, MD, PhD<sup>10</sup>; Mir P, MD, PhD<sup>1,2\*</sup>; COPPADIS Study Group.

Table 1. Motor and non motor evaluations in Parkinson's disease according to the presence of compulsive behaviours.

		CBs negative	CBs positive	P value
Number of subjects	N	569	44	-
Demographic	Sex (M/F)	340/229	27/17	0.95
	Age (Mean $\pm$ SD)	62.56 $\pm$ 9.08	61.30 $\pm$ 9.24	0.31
Family history PD	N	157 (27.59)	13 (29.54)	0.92
Age at onset	Age (Mean $\pm$ SD)	58.07 $\pm$ 9.52	55.50 $\pm$ 10.14	0.07
Disease progression time	Years (Mean $\pm$ SD)	5.50 $\pm$ 4.45	5.88 $\pm$ 4.39	0.39
UPDRS Score (Mean $\pm$ SD)	II OFF	2.71 $\pm$ 1.86	3.24 $\pm$ 2.02	0.13
	II ON	1.72 $\pm$ 1.82	1.65 $\pm$ 2.01	0.77*
	III OFF	22.34 $\pm$ 11.11	27.00 $\pm$ 12.08	0.05*
	III ON	16.11 $\pm$ 8.27	16.28 $\pm$ 7.79	0.97*
	IV	1.92 $\pm$ 2.36	2.72 $\pm$ 2.49	<b>0.04*</b>

Phenotype (undetermined/PIGD/Tremor)	N	89/220/258	8/18/18	0.82
Dominant hemibody	N	30/1/160/99/174/105	2/0/13/4/16/9	0.68
Motor fluctuations	N (%)	179 (31.45)	19 (43.18)	0.15*
Dyskinesias	N (%)	95 (16.69)	11 (25)	0.23*
NMSS	Score (Mean ± SD)	42.46 ± 34.84	60.50 ± 40.36	<b>0.003*</b>
PDSS	Score (Mean ± SD)	115.95 ± 25.92	102.76 ± 25.20	<b>0.004*</b>
Pain	N (%)	330 (57.99)	23 (52.27)	0.43*
REM sleep behaviour disorder	N (%)	217 (38.14)	16 (36.36)	0.83*
BECK (depression yes)	N (%)	282 (49.56)	31 (70.45)	<b>0.007*</b>
BECK- Depression Inventory	Score (Mean ± SD)	8.49 ± 7.24	12.69 ± 7.76	<b>&lt;0.001*</b>
	Subclinic/minor/ major	87/99/96	11/6/14	0.88*
	No depression vs subclinic	287/87	27/11	0.42*
	No depression vs minor	287/99	27/6	<b>0.002*</b>
	No depression vs major	287/96	27/14	0.13*
FOG	Score (Mean ± SD)	3.53 ± 4.45	5.39 ± 5.01	<b>0.009*</b>
MMSE	Score (Mean ± SD)	29.20 ± 1	29.18 ± 1.09	0.97*
PD-CRS	Score (Mean ± SD)	91.74 ± 15.89	91.95 ± 16.19	0.85*
	Non CI/MCI/dementi a	397/164/3	32/9/1	0.22
	Fronto- subcortical	63.87 ± 14.63	64.23 ± 14.06	0.82*
	Posterior cortical	27.89 ± 2.95	27.71 ± 3.27	0.89*

NPI (severity x frequency)	Score (Mean ± SD)	5.67 ± 7.76	9.17 ± 8.43	<b>0.02*</b>
PDQ-39	Score (Mean ± SD)	15.99 ± 12.54	24.85 ± 15.45	<b>&lt;0.001*</b>
WHOQOL-8	Score (Mean ± SD)	7.31 ± 1.59	7.06 ± 1.46	0.625
Results for univariate tests: chi-square test, t-test or Wilcoxon test.				
*Results for multivariate analysis: multivariate linear regression or multivariate logistic regression adjusted by age, years of disease duration.				
CBs: compulsive behaviours, FOG: Freezing of Gait Scale, UPDRS: Unified Parkinson's Disease Rating Scale, N: number of subjects, NMSS: Non Motor Symptoms Scale, NPI: Neuropsychiatry Inventory, PD: Parkinson's disease, PD-CRS: Parkinson's Disease Cognitive Rating Scale, PDQ-39: 39 items Parkinson's Disease Questionnaire, PDSS: Parkinson's Disease Sleep Scale, REM: Rapid Eye Movements, SD: standard deviation, WHOQOL-8: 8 items World Health Organization Quality of Life.				

Table 2. Demographic characteristics of Parkinson's disease according to the presence of impulse control disorders in patients on dopaminergic agonist treatment.

		ICDs negative	ICDs positive	P Value
	N	355	67	-
Demographic	Sex (M/F)	220/135	45/22	0.5
	Age (Mean ± SD)	62.24±8.7	59.34±9.63	<b>0.02</b>
	Culture level <sup>1</sup>	146/108/100	26/24/17	0.68
	Lifestyle <sup>2</sup>	290/15/15/34	51/1/5/7	0.49
	Habitat <sup>3</sup>	43/56/255	6/15/46	0.36
Premorbidity	Historical ICDs or CBs	47 (41.59)	20 (74.07)	<b>0.001</b>
	Premorbid impulsive personality	25 (7.04)	11 (16.41)	<b>0.023</b>

	Family history of ICDs or CBs	24 (6.76)	6 (8.95)	0.7
	Family history of PD	93 (26.19)	21 (31.34)	0.47
Comorbidity	Antidepressant treatment	68 (19.15)	23 (34.32)	<b>0.012*</b>
	Anxiolytic treatment	44 (12.39)	10 (14.92)	0.51*
	Antipsychotic treatment	5 (1.40)	3 (4.47)	0.17*
	Smoke	129 (36.33)	28 (41.79)	0.48
	Alcohol intake	75 (21.12)	13 (18.40)	0.87
Results for univariate tests: chi-square test, t-test or Wilcoxon test.				
*Results for multivariate analysis: multivariate linear regression or multivariate logistic regression adjusted by age, years of disease duration.				
<sup>1</sup> Culture level (Elementary / High School / University), <sup>2</sup> Life style (Married/Married with children/Others/Alone), <sup>3</sup> Habitat (Rural/Semiurban/Urban)				
ICDs: impulse control disorders, CBs: compulsive behaviours, N: number of subjects, M: male, F: female, PD: Parkinson's disease				

Table 3. Motor and non motor evaluations in Parkinson's disease according to the presence of impulse control disorders in patients on dopaminergic agonist treatment.

		ICDs negative	ICDs positive	P value
Number of subjects		355	67	
Family history PD	N	93	21	0.47
Age at onset	Age (Mean ± SD)	57±8.92	53.86±9.72	<b>0.015</b>
Disease progression	Years (Mean ± SD)	6.07±4.71	6.57±3.97	0.1

time				
UPDRS Score (Mean ± SD)	II OFF	2.67±1.86	3.54±2.38	<b>0.001*</b>
	II ON	1.67±1.82	1.9±2.1	0.55*
	III OFF	22.31±10.43	25.46±13.16	<b>0.02*</b>
	III ON	15.59±8.13	15.56±8.05	0.77*
	IV	2.06±2.36	2.6±2.48	0.15*
Phenotype (undetermined/PIGD/Tremor)	N	51/148/156	12/30/25	0.55
Dominant hemibody	N	24/102/52	2/19/12	0.79
Motor fluctuations	N (%)	130 (36.61)	26 (38.80)	0.94*
Dyskinesias	N (%)	70 (19.71)	12 (17.91)	0.53*
NMSS	Score (Mean ± SD)	38.57±30.52	59.51±43	<b>&lt;0.001*</b>
PDSS	Score (Mean ± SD)	115.78±26.26	102.43±26.79	<b>&lt;0.001*</b>
Pain	N (%)	200 (56.33)	39 (58.2)	0.94*
REM sleep behaviour disorder	N (%)	125 (35.2)	29 (43.2)	0.2
BECK (depression yes)	N (%)	153 (43.1)	45 (67.16)	<b>&lt;0.001*</b>
BECK- Depression Inventory	Score (Mean ± SD)	7.73±6.71	12.49±8.25	<b>&lt;0.001*</b>
	Subclinic/minor/major	39/53/61	16/14/15	0.71
	No depression vs subclinic	202/39	22/16	<b>0.001*</b>
	No depression vs minor	202/53	202/61	<b>0.01*</b>
	No depression vs major	22/14	22/15	<b>0.03*</b>
FOG	Score (Mean ± SD)	3.6±4.52	6.18±5.94	<b>&lt;0.001*</b>
MMSE	Score (Mean ± SD)	29.15±1.01	29.24±1.01	0.97*
PD-CRS	Score (Mean ± SD)	92.02±15.81	93.8±16.81	0.8*

NPI (severity x frequency)	Non CI/MCI/dementia	250/79/22	48/16/3	0.84
	Fronto-subcortical	64.16±14.5	65.97±15.64	0.88*
	Posterior cortical	27.86±3.01	27.83±2.57	0.52*
	Score (Mean ± SD)	4.89±6.83	9.36±10.81	<b>&lt;0.001*</b>
PDQ-39	Score (Mean ± SD)	15.08±11.85	23.55±15.1	<b>&lt;0.001*</b>
WHOQOL-8	Score (Mean ± SD)	7.35±1.63	6.98±1.59	0.1*
Results for univariate tests: chi-square test, t-test or Wilcoxon test.				
*Results for multivariate analysis: multivariate linear regression or multivariate logistic regression adjusted by age, years of disease duration.				
ICDs: impulse control disorders, FOG: Freezing of Gait Scale, UPDRS: Unified Parkinson's Disease Rating Scale, N: number of subjects, NMSS: Non Motor Symptoms Scale, NPI: Neuropsychiatry Inventory, PD: Parkinson's disease, PD-CRS: Parkinson's Disease Cognitive Rating Scale, PDQ-39: 39 items Parkinson's Disease Questionnaire, PDSS: Parkinson's Disease Sleep Scale, REM: Rapid Eye Movements, SD: standard deviation, WHOQOL-8: 8 items World Health Organization Quality of Life.				

Table 4. Demographic characteristics of Parkinson's disease according to the presence of impulse control disorders in patients with an age at disease onset under 50 years old.

		ICDs negative	ICDs positive	P value
	N	113	27	
Demographic	Sex (M/F)	79/34	13/14	0.055
	Age (Mean ± SD)	50.56 ± 7.46	49 ± 6.56	0.28
	Culture level <sup>1</sup>	35/30/48	5/16/6	<b>0.004</b>
	Lifestyle <sup>2</sup>	89/6/9/9	20/2/4/1	0.59
	Habitat <sup>3</sup>	11/18/84	1/5/21	0.59
Premorbidity	Historical ICD or CB (%)	32 (28.32)	10 (37.03)	0.53
	Premorbid impulsive	8 (7.08)	6 (22.2)	<b>0.04</b>

	personality (%)			
	Familiar history of ICD or BD (%)	19 (16.8)	1 (3.7)	0.15
	Family history of PD (%)	31 (27.43)	11 (40.74)	0.26
Comorbidity	Antidepressant treatment (%)	20 (18.3)	7 (24.1)	0.53*
	Anxiolytic treatment N (%)	18 (15.9)	5 (18.5)	0.68*
	Antipsychotic treatment N (%)	4 (3.5)	0 (0)	0.99*
	Smoke N (%)	42 (37.7)	7 (25.9)	0.38
	Alcohol intake N (%)	26 (23)	1 (3.7)	<b>0.04</b>
Results for univariate tests: chi-square test, t-test or Wilcoxon test.				
*Results for multivariate analysis: multivariate linear regression or multivariate logistic regression adjusted by age, years of disease duration.				
<sup>1</sup> Culture level (Elementary / High School / University), <sup>2</sup> Life style (Married/Married with children/Others/Alone), <sup>3</sup> Habitat (Rural/Semiurban/Urban)				
ICDs: impulse control disorders, CBs: compulsive behaviour, N: number of subjects, M: male, F: female, PD: Parkinson's disease				

Table 5. Motor and non motor evaluations in Parkinson's disease according to the presence of impulse control disorders in patients with age at onset under 50 years old.

		ICDs negative	ICDs positive	P value
Number of subjects		113	27	-

Family history PD	N	31 (27.4)	11 (40.74)	0.26
Age at onset	Age (Mean $\pm$ SD)	44.37 $\pm$ 5.5	43.44 $\pm$ 5.98	0.47
Disease evolution time	Years (Mean $\pm$ SD)	7.33 $\pm$ 5.9	6.66 $\pm$ 4.37	0.99
UPDRS Score (Mean $\pm$ SD)	II OFF	2.9 $\pm$ 2.12	3.61 $\pm$ 2.21	0.06*
	II ON	1.68 $\pm$ 1.94	1.2 $\pm$ 1.31	0.47*
	III OFF	24.8 $\pm$ 15.52	26.42 $\pm$ 13.33	0.35*
	III ON	15.94 $\pm$ 8.67	16 $\pm$ 5.79	0.98*
	IV	2.8 $\pm$ 2.98	2.52 $\pm$ 2.22	0.66*
Phenotype (undetermined/PIGD/Tremor)	N	18/51/43	5/12/10	0.95
Dominant hemibody	N	6/32/17/32/25	0/7/8/6/6	0.36
Motor fluctuations	N (%)	51 (45.1)	9 (33.3)	0.25*
Dyskinesias	N (%)	26 (23.21)	4 (14.8)	0.33*
NMSS	Score (Mean $\pm$ SD)	44.72 $\pm$ 40.29	65.89 $\pm$ 50.2	<b>0.01*</b>
Pain	N (%)	71 (62.8)	18 (66.6)	0.71*
PDSS	Score (Mean $\pm$ SD)	107.41 $\pm$ 32.56	101.55 $\pm$ 30.85	0.34*
REM sleep behaviour disorder	N (%)	41 (36.28)	13 (48.15)	0.16*
BECK (depression yes)	N (%)	54 (47.7)	15 (55.5)	0.39*
BECK- Depression Inventory	Score (Mean $\pm$ SD)	9.5 $\pm$ 8.55	13.8 $\pm$ 9.8	<b>0.02*</b>
	Subclinic/minor/major	21/10/23	6/4/5	0.6
	No depression vs subclinic	59/21	12/6	0.47*
	No depression vs minor	59/10	12/4	0.32*
	No depression vs major	59/23	12/5	0.79*

FOG	Score (Mean ± SD)	4.24±4.71	7.07±6.25	<b>0.002*</b>
MMSE	Score (Mean ± SD)	29.24±1.01	29.4±0.88	0.59*
PD-CRS	Score (Mean ± SD)	98.088±15.76	101.59±16.79	0.46*
	Non CI/MCI/dementia	95/17/1	24/3/0	0.77
	Fronto-subcortical	69.83±14.93	73.4±15.75	0.38*
	Posterior cortical	28.25±2.89	28.18±2.62	0.67*
NPI (severity x frequency)	Score (Mean ± SD)	7.36±10.26	8.87±10.62	0.51*
PDQ-39	Score (Mean ± SD)	19.69±1.95	25.35±16.03	<b>0.05*</b>
WHOQOL-8	Score (Mean ± SD)	7.07±1.65	6.63±1.76	0.22*
Results for univariate tests: chi-square test, t-test or Wilcoxon test.				
*Results for multivariate analysis: multivariate linear regression or multivariate logistic regression adjusted by age, years of disease duration.				
ICDs: impulse control disorders, FOG: Freezing of Gait Scale, UPDRS: Unified Parkinson's Disease Rating Scale, N: number of subjects, NMSS: Non Motor Symptoms Scale, NPI: Neuropsychiatry Inventory, PD: Parkinson's disease, PD-CRS: Parkinson's Disease Cognitive Rating Scale, PDQ-39: 39 items Parkinson's Disease Questionnaire, PDSS: Parkinson's Disease Sleep Scale, REM: Rapid Eye Movements, SD: standard deviation, WHOQOL-8: 8 items World Health Organization Quality of Life.				

Table 6. Principal investigators and sites included in COPPADIS Study Group.

Principal Investigator; PI's participating site		City
1.	Diego Santos García; Neurology Section, Hospital Arquitecto Marcide, Complejo Hospitalario Universitario de Ferrol (CHUF).	Ferrol (A Coruña)
2.	(1) Oriol de Fàbregues-Boixar Nebot and (2) Jorge Hernández Vara; Movement Disorders Unit, Neurology Service, Hospital Universitario Vall d'Hebron.	Barcelona
3.	Carmen Borrue Fernández; Movement Disorders Unit, Neurology Service, Hospital Infanta Sofía.	Madrid
4.	Pablo Mir Rivera; Movement Disorders Unit, Neurology and	Seville

<b>Principal Investigator; PI's participating site</b>		<b>City</b>
	Clinical Neurophysiology Service, Instituto de Biomedicina de Sevilla, Hospital Universitario Virgen del Rocío, CSIC and Universidad de Sevilla.	
5.	Maria José Martí Domenech; Parkinson's and Movement Disorders Unit, Neurology Service, Instituto Clínico de Neurociencias, Hospital Clínic.	Barcelona
6.	Miquel Aguilar Barberá; Movement Disorders Unit, Hospital Universitario Mutua de Terrassa.	Barcelona
7.	Beatriz Tijero Merino; Functional Neurology and Parkinson's Disease Unit, Hospital de Cruces.	Bilbao
8.	José Chacón Peña; Neurology Unit, Hospital Infanta Luisa.	Seville
9.	(1) Manuel Seijo Martínez and (2) Iria Cabo López; Neurology Section, Hospital de Pontevedra.	Pontevedra
10.	Víctor Puente Pérez; Movement Disorders Unit, Neurology Service, Hospital del Mar.	Barcelona
11.	Inés Legarda Ramiréz; Neurology Service, Hospital Universitario Son Espases.	Palma de Mallorca
12.	Francisco Carrillo Padilla; Neurology Service, Hospital Universitario de Canarias, San Cristóbal de la Laguna.	Santa Cruz de Tenerife
13.	Lydia López Manzanares; Movement Disorders Unit, Neurology Service, Hospital La Princesa.	Madrid
14.	Caridad Valero Merino; Neurology Unit, Hospital Arnau de Vilanova.	Valencia
15.	Jaime Kulisevsky Bojarski; Movement Disorders Unit, Neurology Service, Hospital de Sant Pau.	Barcelona
16.	José Manuel García Moreno; Movement Disorders Unit, Hospital Universitario Virgen Macarena.	Seville
17.	Benito Galeano Bilbao; Neurology Section, Hospital Universitario de Ceuta.	Ceuta
18.	Nuria Caballol Pons; Movement Disorders Unit, Consorci Sanitari Integral, Hospital Moisès Broggi.	Sant Joan Despí

Principal Investigator; PI's participating site	City
19. Mari Cruz Rodríguez Oroz; Hospital Universitario Donostia, Instituto de Investigación Biodonostia.	San Sebastián
20. María Iciar Gastón Zubimendi; Movement Disorders Unit, Neurology Service, Complejo Hospitalario de Navarra.	Pamplona
21. Pilar Sánchez Alonso; Neurology Service, Hospital Puerta de Hierro.	Madrid
22. Esther Cubo Delgado; Neurology Service, Complejo Asistencial Universitario de Burgos.	Burgos
23. Lydia Vela Desojo; Neurology Unit, Fundación Hospital de Alcorcón.	Alcorcón (Madrid)
24. Maria José Catalán Alonso; Movement Disorders Unit, Neurology Service, Hospital Clínico San Carlos.	Madrid
25. Luis Manuel López Díaz; Neurology Section, Hospital de Burela.	Burela (Lugo)
26. Maria Gema Alonso Losada; Neurology Service, Hospital Meixoeiro, Complejo Hospitalario Universitario de Vigo (CHUVI).	Vigo (Pontevedra)
27. Nuria López Ariztegui; Movement Disorders Unit, Complejo Hospitalario de Toledo.	Toledo
28. Mónica Kurtis Urra; Movement Disorders Unit, Neurology Service, Hospital Ruber Internacional.	Madrid
29. Jon Infante Ceberio; Movement Disorders Unit, Neurology Service, Hospital Universitario Marqués de Valdecilla.	Santander
30. Sonia Escalante Arroyo; Neurology Service, Hospital de Tortosa Verge de la Cinta (HTVC).	Tortosa (Tarragona)
31. Juan Carlos Martínez Castrillo; Movement Disorders Unit, Neurology Service, Hospital Ramón y Cajal.	Madrid
32. José Matías Arbelo González; Movement Disorders and Parkinson's Disease Unit, Neurology Service, Hospital Universitario Insular de Gran Canaria.	Las Palmas de Gran Canaria
33. René Ribacoba Montero; Movement Disorders Unit, Neurology	Oviedo

Principal Investigator; PI's participating site	City
34. Jessica González Ardura; Neurology Service, Hospital Universitario Lucus Augusti (HULA).	Lugo
35. Javier López del Val; Movement Disorders Unit, Neurology Service, Hospital Clínico Universitario Lozano Blesa.	Zaragoza
36. María Asunción Ávila Rivera; Movement Disorders Unit, Consorci Sanitari Integral, Hospital General de L'Hospitalet.	L'Hospitalet de Llobregat
37. Hortensia Alonso Navarro; Neurology Section, Hospital Universitario del Sureste, Madrid.	Madrid
38. Berta Solano Vila; Neurology Service, Hospital Josep Trueta and Parc Martí i Juliá, Girona.	Girona
39. Juan García Caldentey; Neurology Unit, Hospital Quirón Palmaplanas.	Palma de Mallorca
40. Ana Rojo Sebastián; Parkinson's and Abnormal Movement Unit, Neurology Service, Hospital Universitario Príncipe de Asturias.	Alcalá de Henares (Madrid)
41. Silvia Martí Martínez; Neurology Service, Hospital General de Alicante.	Alicante
42. José Andrés Domínguez Morán; Neurology Unit, Hospital de la Rivera.	Alcira (Valencia)
43. Irene Martínez Torres; Movement Disorders Unit, Neurology Service, Hospital La Fe.	Valencia
44. María Álvarez Sauco; Neurology Service, Hospital General Universitario de Elche.	Elche (Alicante)
45. Cristina Prieto Jurczynska; Movement Disorders Unit, Hospital Infanta Elena-Hospital Rey Juan Carlos-Hospital Collado Villalba, Madrid.	Madrid

The local Ethics Committee at each center approved the participation in the study.