Supplementary Materials

Characterization of recessive Parkinson's disease in a large multicenter study

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Supplementary TABLE 1. Generalised linear models (GLM) results for the 15 variables of interest

part: 1/5	Intercept	Sex (reference: F)				Mutation status (reference: PD-NM)			
		Coefficient ± SEM	Cohen's f2	*p*-value	*p*-value adjusted ¥	Coefficient ± SEM	Cohen's f2	*p*-value	*p*-value adjusted ¥
Dystonia at onset	-0.35 ± 0.33	-0.16 ± 0.18	<0.001	0.7041	0.8487	-0.79 ± 0.66	0.001	0.4248	0.4645
Akinesia at onset	0.95 ± 0.27	0.04 ± 0.14	0.001	0.2950	0.7374	-1.30 ± 0.52	0.015	0.0001*	0.0003*
Tremor at onset	-0.03 ± 0.26	0.04 ± 0.13	<0.001	0.5964	0.8257	1.04 ± 0.54	0.007	0.0030*	0.0076*
Micrographia at onset	-1.16 ± 0.28	0.09 ± 0.14	<0.001	0.6055	0.8257	-0.41 ± 0.62	0.007	0.0047*	0.0100*
Bradykinesia	2.36 ± 0.85	-0.40 ± 0.37	0.002	0.4026	0.8257	0.19 ± 1.62	0.002	0.4335	0.4645
Rigidity	2.36 ± 0.62	0.33 ± 0.27	0.002	0.2645	0.7374	0.24 ± 1.41	<0.001	0.7738	0.7738
Tremor	0.30 ± 0.36	0.04 ± 0.15	<0.001	0.8066	0.8487	1.45 ± 0.82	0.002	0.0480*	0.0720
Asymmetry	3.70 ± 0.87	0.05 ± 0.36	0.001	0.5544	0.8257	-2.23 ± 1.35	0.010	0.0002*	0.0005*
Dyskinesia	0.05 ± 0.54	-0.26 ± 0.19	0.003	0.1490	0.7374	-2.08 ± 0.88	0.020	0.0001*	0.0005*
Motor fluctuations	-0.03 ± 0.53	0.05 ± 0.19	<0.001	0.8487	0.8487	-0.50 ± 0.86	0.041	<0.0001*	<0.0001*
Dysautonomia	-0.86 ± 0.52	-0.21 ± 0.21	0.002	0.1352	0.7374	-1.90 ± 0.95	0.086	<0.0001*	<0.0001*
Dementia	-2.93 ± 0.70	0.11 ± 0.27	<0.001	0.7969	0.8487	-1.31 ± 1.79	0.009	0.0087*	0.0144*
Levodopa responsiveness	-0.53 ± 0.68	0.11 ± 0.26	0.001	0.5672	0.8257	5.02 ± 1.98	0.007	0.1135	0.1547
Hoehn&Yahr ON‡	1.84 ± 0.19	-0.12 ± 0.07	0.002	0.2813	0.7374	-0.59 ± 0.40	0.003	0.1297	0.1621
UPDRS-Part III ON‡	9.17 ± 2.53	1.80 ± 0.98	0.005	0.0308*	0.4625	-3.88 ± 4.72	0.008	0.0081*	0.0144*

part: 2/5	Age at onset				Disease duration (years)			
	Coefficient ± SEM	Cohen's f2	*p*-value	*p*-value adjusted ¥	Coefficient ± SEM	Cohen's f2	*p*-value	*p*-value adjusted ¥
Dystonia at onset	-0.03 ± 0.01	0.014	0.0001*	0.0005*				
Akinesia at onset	-0.01 ± 0.01	0.003	0.0731	0.1829				
Tremor at onset	0.01 ± 0.01	0.001	0.2149	0.2930				
Micrographia at onset	0.01 ± 0.01	0.002	0.0935	0.2004				
Bradykinesia	0.02 ± 0.02	0.003	0.2102	0.2930	-0.02 ± 0.04	0.002	0.1849	0.1849
Rigidity	-0.01 ± 0.01	<0.001	0.9310	0.9851	-0.02 ± 0.04	0.002	0.1623	0.1785
Tremor	0.01 ± 0.01	0.002	0.1850	0.2930	0.02 ± 0.02	0.003	0.0301*	0.0413*
Asymmetry	-0.01 ± 0.02	0.004	0.1122	0.2104	0.20 ± 0.10	-0.001	0.1012	0.1237
Dyskinesia	-0.03 ± 0.01	<0.001	0.9851	0.9851	-0.01 ± 0.03	0.119	<0.0001*	<0.0001*
Motor fluctuations	-0.03 ± 0.01	0.004	0.0326*	0.1222	-0.08 ± 0.03	0.077	<0.0001*	<0.0001*
Dysautonomia	-0.01 ± 0.01	0.006	0.0079*	0.0396*	-0.04 ± 0.04	0.034	<0.0001*	<0.0001*
Dementia	0.00 ± 0.01	0.002	0.4413	0.5516	0.03 ± 0.03	0.007	0.0265*	0.0413*
Levodopa responsiveness	0.02 ± 0.02	0.003	0.5417	0.6250	0.23 ± 0.11	0.070	<0.0001*	<0.0001*
Hoehn&Yahr ON‡	-0.01 ± 0.00	0.005	0.0589	0.1767	-0.02 ± 0.01	0.102	<0.0001*	<0.0001*
UPDRS-Part III ON‡	0.11 ± 0.06	0.026	<0.0001*	<0.0001*	0.12 ± 0.16	0.064	<0.0001*	<0.0001*

part: 3/5

	L-DOPA group (reference: no L-DOPA)				Mutation status : Sex (references: PD-NM / F)			
	Coefficient ± SEM	Cohen's f2	*p*-value	*p*-value adjusted ¥	Coefficient ± SEM	Cohen's f2	*p*-value	*p*-value adjusted ¥
Dystonia at onset					0.53 ± 0.41	0.001	0.1918	0.8154
Akinesia at onset					0.47 ± 0.31	0.002	0.1304	0.8154
Tremor at onset					0.16 ± 0.33	<0.001	0.6382	0.8154
Micrographia at onset					-0.12 ± 0.38	<0.001	0.7481	0.8154
Bradykinesia	0.92 ± 0.37	0.008	0.0058*	0.0105*	0.71 ± 0.87	<0.001	0.4076	0.8154
Rigidity	0.68 ± 0.30	0.005	0.0342*	0.0538	-0.28 ± 0.71	<0.001	0.6898	0.8154
Tremor	0.14 ± 0.17	0.001	0.3852	0.4905	-0.03 ± 0.41	<0.001	0.9417	0.9417
Asymmetry	-0.79 ± 0.48	<0.001	0.4013	0.4905	0.38 ± 0.63	<0.001	0.5411	0.8154
Dyskinesia	1.20 ± 0.27	0.039	<0.0001*	<0.0001*	0.12 ± 0.40	<0.001	0.7588	0.8154
Motor fluctuations	1.24 ± 0.28	0.034	<0.0001*	<0.0001*	-0.32 ± 0.39	0.001	0.4112	0.8154
Dysautonomia	1.29 ± 0.27	0.036	<0.0001*	0.0001*	-0.29 ± 0.45	<0.001	0.5247	0.8154
Dementia	0.35 ± 0.36	<0.001	0.8724	0.8887	-0.47 ± 0.95	0.001	0.6246	0.8154
Levodopa responsiveness	0.81 ± 0.28	0.005	0.0012*	0.0032*	0.35 ± 0.87	<0.001	0.6819	0.8154
Hoehn&Yahr ON‡	0.32 ± 0.10	0.014	0.0019*	0.0042*	0.34 ± 0.18	0.005	0.0569	0.8154
UPDRS-Part III ON‡	0.62 ± 1.27	<0.001	0.8887	0.8887	0.70 ± 2.30	<0.001	0.7611	0.8154

part: 4/5

	Mutation status : Age at onset (reference: PD-NM)				Mutation status : disease duration (years) (reference: PD-NM)			
	Coefficient ± SEM	Cohen's f2	*p*-value	*p*-value adjusted ¥	Coefficient ± SEM	Cohen's f2	*p*-value	*p*-value adjusted ¥
Dystonia at onset	0.01 ± 0.02	<0.001	0.5717	0.7795				
Aakinesia at onset	0.01 ± 0.01	0.001	0.4259	0.6713				
Tremor at onset	-0.02 ± 0.02	0.001	0.2198	0.6593				
Micrographia at onset	0.00 ± 0.02	<0.001	0.9108	0.9226				
Bradykinesia	-0.02 ± 0.04	<0.001	0.6777	0.8471	0.02 ± 0.04	0.001	0.6725	0.7398
Rigidity	0.00 ± 0.03	<0.001	0.9226	0.9226	0.02 ± 0.04	<0.001	0.6159	0.7398
Tremor	-0.04 ± 0.02	0.002	0.0296*	0.2188	0.04 ± 0.03	0.002	0.1376	0.3028
Asymmetry	0.03 ± 0.03	0.002	0.4475	0.6713	-0.14 ± 0.05	0.002	0.0078*	0.0431*
Dyskinesia	0.02 ± 0.02	0.002	0.3109	0.6713	0.05 ± 0.03	0.004	0.0930	0.2584
Motor fluctuations	-0.02 ± 0.02	0.001	0.4406	0.6713	0.03 ± 0.02	<0.001	0.2991	0.4700
Dysautonomia	0.05 ± 0.02	0.008	0.0130*	0.1943	-0.03 ± 0.03	0.003	0.1836	0.3367
Dementia	0.07 ± 0.04	<0.001	0.1267	0.4752	-0.01 ± 0.04	0.001	0.7848	0.7848
Levodopa responsiveness	-0.10 ± 0.05	-0.002	0.0438*	0.2188	-0.19 ± 0.06	0.006	0.0042*	0.0431*
Hoehn&Yahr ON‡	0.01 ± 0.01	0.001	0.3470	0.6713	0.02 ± 0.01	0.004	0.0940	0.2584
UPDRS-Part III ON‡	0.03 ± 0.11	<0.001	0.8124	0.9226	0.08 ± 0.14	<0.001	0.5489	0.7398

part: 5/5	Age at onset : disease duration (years)				Mutation status : L-DOPA group (references: no L-DOPA / PD-NM)			
	Coefficient ± SEM	Cohen's f2	*p*-value	*p*-value adjusted ¥	Coefficient ± SEM	Cohen's f2	*p*-value	*p*-value adjusted ¥
Dystonia at onset								
Akinesia at onset								
Tremor at onset								
Micrographia at onset								
Bradykinesia	0.00 ± 0.00	<0.001	0.8056	0.8056	0.11 ± 0.88	<0.001	0.8997	0.9838
Rigidity	0.00 ± 0.00	0.001	0.2721	0.4276	-0.60 ± 0.74	<0.001	0.4174	0.6151
Tremor	0.00 ± 0.00	<0.001	0.7035	0.8056	-0.04 ± 0.43	<0.001	0.9355	0.9838
Asymmetry	0.00 ± 0.00	-0.002	0.2099	0.3848	1.29 ± 0.73	0.002	0.0754	0.2764
Dyskinesia	0.00 ± 0.00	0.007	0.0036*	0.0098*	0.01 ± 0.50	<0.001	0.9838	0.9838
Motor fluctuations	0.00 ± 0.00	0.032	<0.0001*	<0.0001*	-0.38 ± 0.49	<0.001	0.4474	0.6151
Dysautonomia	0.00 ± 0.00	0.014	0.0020*	0.0072*	-1.39 ± 0.50	0.008	0.0070*	0.0386*
Dementia	0.00 ± 0.00	<0.001	0.7806	0.8056	-3.19 ± 1.20	0.006	0.0017*	0.0190*
Levodopa responsiveness	0.00 ± 0.00	0.002	0.5097	0.7008	0.95 ± 0.99	0.003	0.3359	0.6151
Hoehn&Yahr ON‡	0.00 ± 0.00	0.035	<0.0001*	<0.0001*	-0.28 ± 0.25	0.002	0.2780	0.6151
UPDRS-Part III ON‡	0.01 ± 0.00	0.005	0.0451*	0.0993	-2.20 ± 2.77	0.001	0.4285	0.6151

Coefficients and standard error (SE) were extracted from complete GLMs with all interactions. Complete GLMs included sex, mutation status, age-at-onset, disease duration, L-DOPA group, mutation status:sex, mutation status:age-at-onset, mutation status:disease duration, mutation status:L-DOPA group and age-at-onset:disease for all 15 variables except for onset variables for which effects involving disease duration and L-DOPA group were not included

‡ Linear models were used to compare clinical features between *PRKN*-PD and PD-NM; generalised linear models (GLM) with logit links and Bernouilli distributions were used otherwise

* $p<0.05$

¥ p corrected for multiple testing by the Benjamini-Hochberg procedure

Supplementary TABLE 2. Comparison of the demographic and clinical characteristics of patients with Parkinson's disease carrying *PINK1* (*PINK1*-PD) and *PRKN* mutations (*PRKN*-PD)

Characteristics	*PINK1*-PD (*n* = 33)	*PRKN*-PD (*n* = 241)	*p* value
Demographic characteristics			
Sex (% male)	17/33 (51.5%)	125/241 (51.9%)	1
Age at onset (SD), year	34.6 (12.2)	31.3 (10.9)	0.20
Age at examination (SD) year	51.9 (15.1)	45.3 (13.0)	0.04*
Disease duration (SD), year	17.3 (12.5)	14.2 (10.4)	0.20
Clinical characteristics			
Dystonia at onset	18/20 (90%)	38/209 (18.2%)	<0.0001*
Akinesia at onset	11/17 (42.1%)	102/214 (47.7%)	0.21
Tremor at onset	2/12 (16.7%)	146/213 (68.5%)	0.0005*
Micrographia at onset	3/17 (17.7%)	43/211 (20.4%)	1
Bradykinesia	32/32 (100%)	209/218 (95.9%)	0.30
Rigidity	31/31 (100%)	203/214 (94.9%)	0.37
Tremor	27/31 (87.1%)	176/215 (81.9%)	0.62
Asymmetry	14/17 (82.4%)	188/206 (91.3%)	0.21
Dyskinesia	14/15 (93.3%)	100/185 (54.1%)	0.0024*
Motor fluctuations	11/15 (66.7%)	85/184 (46.2%)	0.059
Dysautonomia	13/18 (72.2%)	39/199 (19.6%)	<0.0001*
Dementia	7/28 (25%)	6/159 (3.8%)	0.0007*

Demographic and clinical characteristics are expressed as the mean and standard deviation for continuous variables and as counts and percentages for categorical variables, independently for each group. These characteristics were compared between groups using Welch's *t*-tests for continuous variables and Fisher's exact tests for categorical variables.

* $p<0.05$

Supplementary TABLE 3. The French clinicians' network for Parkinson's disease genetics (the PDG group) members

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