

Table e-1. Cohort Clinical Characteristics

Cohort	BCM1	BCM2	UMB	PPMI	PDBP	PROPARK	PROBAND	OSLO
Subjects, n	199	83	375	307	429	136	1641	42
Male, n (%)	124 (62.3%)	56 (67.5%)	249 (66.4%)	210 (68.4%)	254 (59.2%)	94 (69.1%)	1,060 (64.6%)	31 (73.8%)
Age at evaluation, mean (SD)	60.6 (10.3)	62.5 (10.1)	66.7 (9.5)	63.7 (9.7)	64.6 (9.3)	64.9 (7.5)	67.6 (9.1)	65.6 (9.2)
Age at onset, mean (SD)	53.6 (9.8)	56.9 (10.0)	57.4 (10.5)	59.5 (9.8)	57.6 (11.2)	56.4 (8.9)	64.5 (9.6)	57.1 (9.7)
Disease duration, mean (SD)	5.2 (4.7)	4.4 (3.7)	4.8 (4.6)	1.9 (1.8)	6.9 (7.5)	8.5 (4.8)	3.2 (3.0)	8.5 (6.0)
TD subtype, n (%)	109 (54.8)	55 (66.3)	172 (45.9)	217 (70.7)	164 (38.2)	73 (53.7)	762 (46.4)	18 (42.9)
PIGD subtype, n (%)	72 (36.2)	25 (30.1)	169 (45.1)	55 (17.9)	217 (50.6)	47 (34.6)	659 (40.2)	15 (35.7)
Subtype ratio, mean (SD)	0.25 (0.9)	0.31 (0.9)	0.15 (1.1)	0.55 (0.9)	-0.1 (0.9)	0.22 (0.8)	0.02 (0.9)	0.21 (1.2)

BCM1: Baylor College of Medicine DNA bank with UPDRS; BCM2 = Baylor College of Medicine DNA bank with MDS-UPDRS; UMD = University of Maryland cohort; PPMI = Parkinson's Progression Markers Initiative; PDBP = Parkinson's Disease Biomarkers Program; PROPARK = Profiling Parkinson's disease (Netherlands); PROBAND = Tracking Parkinson's Study (United Kingdom); OSLO = University of Oslo (Norway). PIGD: Postural instability/gait difficulty PD motor subtype, TD: tremor-dominant PD motor subtype.

Table e-3. Top GWAS results for PD subtype (TD vs. PIGD)

chr: position	SNP	Gene	Allele	Freq	Effect	SE	P-value	I ²	HetP	Direction
1: 47557933	<i>rs116504637</i>	<i>CYP4Z1</i>	T/G	0.74	0.35	0.07	9.83E-07	12.9	0.33	+++++++-
5: 161678799	<i>rs11949046</i>	<i>GABRG2</i>	T/C	0.89	0.54	0.11	1.57E-06	31	0.21	++??+++
16: 19502663	<i>rs78926797</i>	<i>TMC5</i>	A/C	0.60	-0.3	0.06	2.08E-06	0	0.8	-----
6: 125107499	<i>rs6932127</i>	<i>NKAIN2</i>	T/C	0.89	-0.46	0.1	3.01E-06	20.7	0.27	--+?---
11: 22583068	<i>rs55971529</i>	<i>FANCF</i>	A/G	0.97	-1.08	0.23	3.95E-06	51.6	0.1	+????---
1: 77190938	<i>rs988295487</i>	<i>ST6GALNAC3</i>	C/G	0.96	-0.84	0.18	4.98E-06	16.8	0.31	--???---
16: 82279626	<i>rs13330839</i>	<i>MPHOSPH6</i>	A/G	0.87	-0.47	0.1	7.00E-06	42.1	0.12	+++??---

The Allele column displays A1/A2, with A1 denoting the reference allele for the frequency (Freq) and effect. Direction of association shown (left to right) for BCM1, BCM2, OSLO, PDBP, PPMI, PROBAND, PROPARK, and UMD. For assessment of heterogeneity, the I² statistic and associated p-value (HetP) is provided.

Table e-4. Top GWAS results for tremor/PIGD subtype ratio

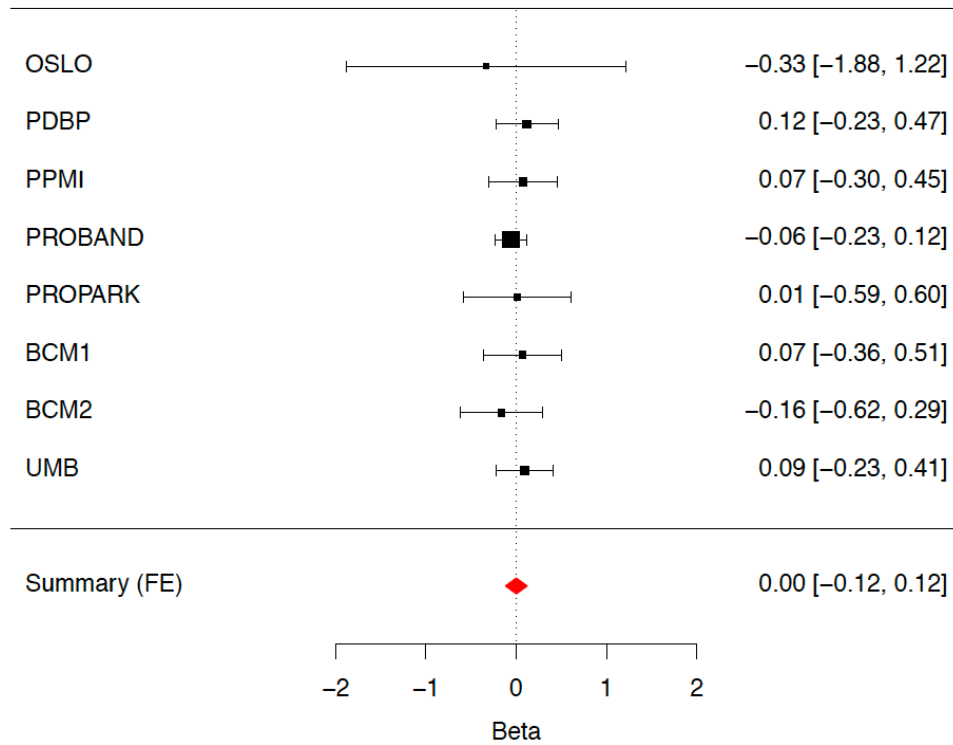
chr: position	SNP	Gene	Allele	Freq	Effect	SE	P-value	I ²	HetP	Direction
4: 5418485	<i>rs2301857</i>	<i>STK32B</i>	T/C	0.12	-0.19	0.04	6.60E-07	36	0.14	-+-----
21: 20786475	<i>rs79890063</i>	none	A/C	0.12	-0.22	0.04	6.96E-07	0	0.58	---+??---
10: 103048995	<i>rs12242050</i>	<i>BTRC</i>	T/G	0.76	-0.14	0.03	8.44E-07	13.8	0.32	-++-----
4: 82616045	<i>rs6535273</i>	<i>RASGEF1B</i>	T/C	0.39	0.11	0.02	1.37E-06	0	0.96	+++++++
8: 8387903	<i>rs10109703</i>	<i>SGK223</i>	A/C	0.64	-0.13	0.03	1.44E-06	16.5	0.31	---??---
13: 110127965	<i>rs17488950</i>	<i>LINC00676</i>	T/C	0.07	-0.27	0.06	1.46E-06	19.5	0.29	-+--??---
4: 86019236	<i>rs76377494</i>	<i>WDFY3-AS2</i>	T/C	0.07	-0.22	0.05	1.89E-06	0	0.6	--+--+---
22: 46008464	<i>rs9626407</i>	<i>FBLN1</i>	A/G	0.04	-0.35	0.07	1.97E-06	0	0.59	---??-+-
12: 62440045	<i>rs116917617</i>	<i>FAM19A2</i>	T/C	0.98	-0.46	0.1	2.11E-06	0	0.45	---??---
19: 14878196	<i>rs538015403</i>	<i>EMR3</i>	A/G	0.02	-0.41	0.09	2.56E-06	40	0.11	-----
7: 148211886	<i>rs2717804</i>	<i>C7orf33</i>	A/G	0.36	-0.12	0.03	2.67E-06	0	0.45	---??---
7: 5794044	<i>rs6958272</i>	<i>RNF216</i>	T/C	0.92	-0.22	0.05	3.01E-06	0	0.58	+--??---
16: 15972631	<i>rs11644635</i>	<i>FOPNL</i>	T/C	0.39	-0.13	0.03	3.14E-06	25.5	0.24	+++??---
4: 116121350	<i>rs2892663</i>	<i>NDST4</i>	T/C	0.5	0.1	0.02	5.73E-06	32.4	0.17	++++-+++
8: 22906180	<i>rs7834008</i>	<i>TNFRSF10B</i>	T/C	0.79	0.14	0.03	5.98E-06	26.2	0.22	++-+++++
5: 5224692	<i>rs2913614</i>	<i>ADAMTS16</i>	A/T	0.54	0.15	0.03	6.33E-06	0	0.42	+++??+++
2: 72300987	<i>rs143548133</i>	<i>CYP26B1</i>	T/C	0.01	0.57	0.13	7.02E-06	11.2	0.34	+--??+-+
6: 134657949	<i>rs9483680</i>	<i>SGK1</i>	A/C	0.9	-0.19	0.04	7.02E-06	0	0.76	-+--??---
11: 132873644	<i>rs2336592</i>	<i>OPCML</i>	C/G	0.63	-0.12	0.03	7.82E-06	0	0.61	---??---
1: 105497011	<i>rs17015314</i>	none	A/G	0.88	-0.17	0.04	7.90E-06	0	0.44	---??---
3: 75446661	<i>rs113942635</i>	<i>FAM86DP</i>	T/C	0.01	0.81	0.18	8.00E-06	0	0.5	--??++++
10: 56421400	<i>rs117238693</i>	<i>PCDH15</i>	T/C	0.98	0.43	0.1	8.04E-06	0	0.88	+--+?+++
11: 103916643	<i>rs77942836</i>	<i>PDGFD</i>	A/G	0.02	-0.53	0.12	8.11E-06	47	0.09	---??--+
2: 57141732	<i>rs56242312</i>	none	A/G	0.9	-0.19	0.04	8.18E-06	12.3	0.34	-++??---
19: 45887928	<i>rs7257687</i>	<i>PPP1R13L</i>	T/C	0.03	-0.30	0.07	8.30E-06	0	0.89	-++-----
13: 87927123	<i>rs72636490</i>	<i>MIR4500HG</i>	A/C	0.08	-0.21	0.05	8.59E-06	22.6	0.26	---??---
14: 47229012	<i>rs75477320</i>	<i>RPL10L</i>	T/C	0.13	0.16	0.04	9.07E-06	40.2	0.11	-+++++++
18: 5197857	<i>rs80164227</i>	<i>C18orf42</i>	A/G	0.97	-0.43	0.1	9.15E-06	8.9	0.34	+--??---
17: 72542970	<i>rs118076379</i>	<i>CD300LD</i>	A/G	0.01	0.59	0.13	9.49E-06	0	0.69	+++??+++
3: 142015590	<i>rs1552340</i>	<i>XRN1</i>	A/G	0.42	0.1	0.02	9.73E-06	41.8	0.1	+++--+++
7: 132040533	<i>rs66792854</i>	<i>PLXNA4</i>	A/G	0.06	0.25	0.06	9.96E-06	0	0.45	+++??+++

The Allele column displays A1/A2, with A1 denoting the reference allele for the frequency (Freq) and effect. Direction of association shown (left to right) for BCM1, BCM2, OSLO, PDBP, PPMI, PROBAND, PROPARK, and UMD. For assessment of heterogeneity, the I² statistic and associated p-value (HetP) is provided.

Table e-5. ET-risk variant associations with PD motor subtype.

chr: position	SNP	Gene	Allele	Freq	Subtype (TD vs. PIGD)			Subtype Ratio		
					Effect	SE	P	Effect	SE	P
4: 5128159	<i>rs10937625</i>	<i>STK32B</i>	T/C	0.75	0.02	0.07	0.79	-0.01	0.03	0.78
4: 24362541	<i>rs17590046</i>	<i>PPARG</i> <i>CIA</i>	T/C	0.8	-0.08	0.08	0.3	-0.02	0.03	0.52
10: 68845715	<i>rs12764057</i>	<i>CTNNA3</i>	T/G	0.62	0.06	0.07	0.35	-0.04	0.03	0.14
10: 68850419	<i>rs10822974</i>	<i>CTNNA3</i>	A/G	0.54	0.06	0.06	0.31	-0.05	0.03	0.07
10: 68917164	<i>rs7903491</i>	<i>CTNNA3</i>	A/G	0.45	0.09	0.06	0.16	-0.04	0.03	0.14

Figure e-1. PD genetic risk score association with motor subtype (TD vs. PIGD).



Meta-analysis evaluating for potential association of our genetic risk score and categorically determined PD motor subtypes in all available cohorts. The error bars represent 95% confidence intervals. The size of the black squares represents the effect size from each cohort. The combined estimate for all cohorts is represented by the red diamond with the width of the diamond representing the 95% confidence interval bounds. The summary effect = 0.00157 (p=0.979).