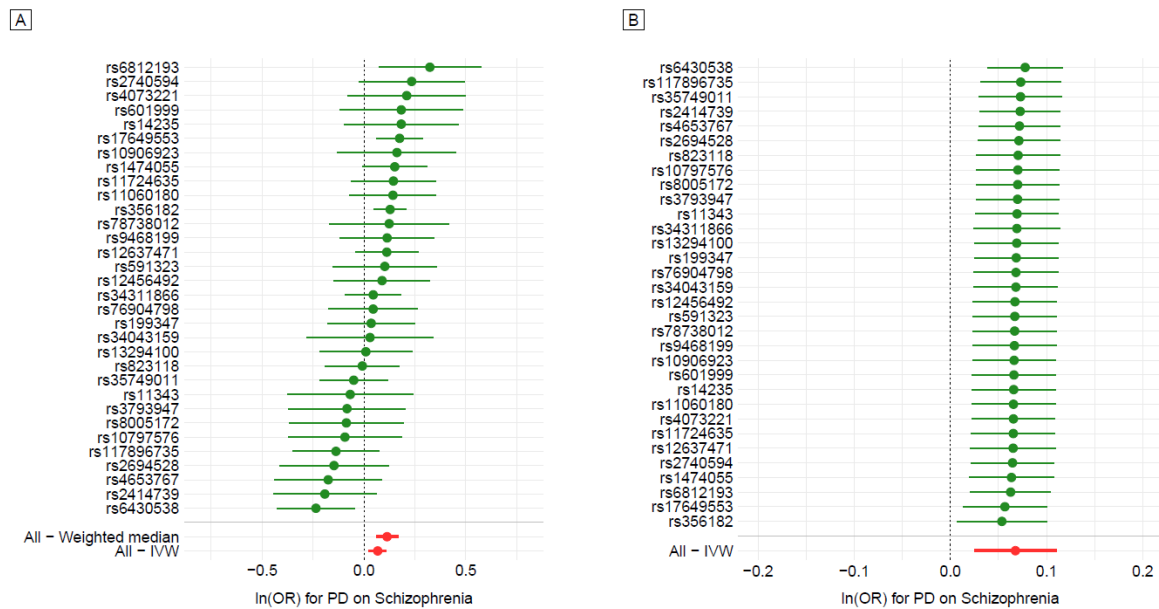


Supplementary Information

Supplementary Figure S1. Forest and leave-one-out plots showing association with schizophrenia for each genetic instrument of Parkinson's disease (PD)

(A) Forest plot using 32 genetic instruments (PD) [1]. (B) Leave-one-out plot using 32 genetic instruments (PD) [1].



Supplementary Table S1. Genome-wide association studies used in this study.

Author	Consortium	No. of cases	No. of controls	No. of SNPs	Population	Sample size	Trait	Year
Simon-Sanchez [2]	NA	1,713	3,978	453,218	European	5,691	Parkinson's disease	2009
Chang [1]	IPDGC	6,476	302,042	-	European	308,518	Parkinson's disease	2017
Ripke [3]	PGC	35,476	46,839	9,444,231	Mixed	82,315	Schizophrenia	2014
Demontis [4]	PGC	20,183	35,191	8,047,420	European	55,374	Attention deficit hyperactivity disorder	2017
Grove [5]	PGC	18,382	27,969	6,440,259	European	46,351	Autism spectrum disorders	2017
Sklar [6]	PGC	7,481	9,250	2,427,221	European	16,731	Bipolar disorder	2011
Sullivan [7]	PGC	9,240	9,519	1,235,110	European	18,759	Major depressive disorder	2013
Lambert [8]	IGAP	17,008	37,154	7,055,882	European	54,162	Alzheimer's disease	2013
Olfson [9]	NA	1,897	1,932	917,030	Mixed	3,829	Alcohol dependence	2012
Furberg [10]	TAG	NA	NA	2,459,119	European	68,028	Cigarettes smoked per day	2010
Watanabe [11]	UK Biobank	NA	NA	9,567,039	European	126,632	Cannabis use - Ever taken cannabis	2019

SNP—single nucleotide polymorphism; IPDGC—International Parkinson's Disease Genomics Consortium; PGC—Psychiatric Genomics Consortium; IGAP—International Genomics of Alzheimer's Project; TAG—Tobacco, Alcohol and Genetics Consortium; NA—not available

Supplementary Table S2. Two-sample Mendelian randomization results of Parkinson's disease [2] (exposure trait) and schizophrenia [3] (outcome trait) using inverse variance weighting (IVW) and weighted median (WM).

		Main Mendelian randomization result (IVW)			Heterogeneity (IVW)			Sensitivity (WM)	
		No. of SNPs	OR (95% CI)	<i>p</i>	Q (Qdf)	Q val	<i>I</i> ² (%)	OR (95% CI)	<i>p</i>
P threshold for PD GWAS	5×10 ⁻⁸	4	1.10 (1.05-1.15)	3.49×10 ⁻⁵	2.54 (3)	0.47	0	1.09 (1.02-1.15)	3.77×10 ⁻³
	5×10 ⁻⁷	5	1.10 (1.06-1.14)	7.00×10 ⁻⁷	2.89 (4)	0.58	0	1.08 (1.02-1.14)	3.13×10 ⁻³
	5×10 ⁻⁶	14	1.06 (1.03-1.09)	6.64×10 ⁻⁵	15.35 (13)	0.29	15	1.05 (1.01-1.10)	7.10×10 ⁻³

SNPs—single nucleotide polymorphisms; PD—Parkinson's disease; GWAS—genome-wide association studies; OR—odds ratio; CI—confidence interval; Q—Cochran's heterogeneity statistic; Qdf—the degrees of freedom; *I*²—100%×(Q - Qdf)/Q [12].

Supplementary Table S3. Two-sample Mendelian randomization results of schizophrenia [3] (exposure trait) and Parkinson's disease [2] (outcome trait) using inverse variance weighting (IVW) and weighted median (WM).

		Main Mendelian randomization result (IVW)			Heterogeneity (IVW)			Sensitivity (WM)	
		No. of SNPs	OR (95% CI)	<i>p</i>	Q (Qdf)	Q val	<i>I</i> ² (%)	OR (95% CI)	<i>p</i>
P threshold for SCZ GWAS	5×10 ⁻⁸	47	1.09 (0.91-1.28)	0.31	40.66 (46)	0.70	0	1.17 (0.89-1.45)	0.19
	5×10 ⁻⁷	66	1.07 (0.91-1.23)	0.40	62.53 (65)	0.56	0	1.15 (0.88-1.42)	0.24
	5×10 ⁻⁶	102	1.03 (0.89-1.17)	0.72	111.30 (101)	0.23	9	1.12 (0.91-1.34)	0.24

SCZ—schizophrenia; GWAS—genome-wide association studies; SNPs—single nucleotide polymorphisms; OR—odds ratio; CI—confidence interval; Q—Cochran's heterogeneity statistic; Qdf—the degrees of freedom; *I*²—100%×(Q - Qdf)/Q [12]

Supplementary Table S4. Two-sample Mendelian randomization results of schizophrenia [3] (exposure trait) and Parkinson's disease [2] (outcome trait) using MR-Egger.

		MR-Egger			Heterogeneity (Egger)			Pleiotropy (Egger)	
		No. of SNPs	OR (95% CI)	<i>p</i>	Q (Qdf)	Q val	<i>I</i> ² (%)	Intercept OR (95% CI)	<i>p</i>
P threshold for SCZ GWAS	5×10 ⁻⁸	47	0.58 (-0.01-1.18)	0.30	40.05 (45)	0.68	0	1.05 (0.97-1.13)	0.23
	5×10 ⁻⁷	66	0.82 (0.13-1.52)	0.65	63.14 (64)	0.51	0	1.02 (0.96-1.08)	0.54
	5×10 ⁻⁶	102	0.92 (0.24-1.60)	0.82	112.31 (100)	0.19	11	1.01 (0.96-1.06)	0.76

SCZ—schizophrenia; GWAS—genome-wide association studies; OR—odds ratio; CI, confidence interval; Q, Cochran's heterogeneity statistic; Qdf, the degrees of freedom; *I*², 100%×(Q - Qdf)/Q [12]

Supplementary Table S5. Two-sample Mendelian randomization results of Parkinson's disease [2] (exposure trait) and schizophrenia [3] (outcome trait) using MR-Egger.

		MR-Egger			Heterogeneity (Egger)			Pleiotropy (Egger)	
		No. of SNPs	OR (95% CI)	<i>p</i>	Q (Qdf)	Q val	<i>I</i> ² (%)	Intercept OR (95% CI)	<i>p</i>
P threshold for PD GWAS	5×10 ⁻⁸	4	0.94 (0.76-1.12)	0.61	1.18 (2)	0.56	0	1.05 (0.99-1.11)	0.25
	5×10 ⁻⁷	5	0.98 (0.81-1.15)	0.84	2.11 (3)	0.55	0	1.03 (0.98-1.09)	0.28
	5×10 ⁻⁶	14	1.07 (0.94-1.21)	0.30	16.60 (12)	0.17	28	1.00 (0.97-1.03)	0.88

PD, Parkinson's disease; GWAS, genome-wide association studies; OR, odds ratio; CI, confidence interval; Q, Cochran's heterogeneity statistic; Qdf, the degrees of freedom; *I*², 100%×(Q - Qdf)/Q [12]

Supplementary Table S6. Two-sample Mendelian randomization results of Parkinson's disease[1] (exposure trait) and schizophrenia[3] (outcome trait) using IVW and WM after removing outliers that exhibit pleiotropy detected by MR-PRESSO.

		Main Mendelian randomization Result (IVW)			Heterogeneity (IVW)			Sensitivity (WM)	
		No. of SNPs	OR (95% CI)	<i>p</i>	Q (Qdf)	Q val	<i>I</i> ² (%)	OR (95% CI)	<i>p</i>
P threshold for PD GWAS	5×10 ⁻⁸	32	1.07 (1.02-1.12)	1.81×10 ⁻³	45.43 (31)	0.05	32	1.12 (1.06-1.18)	2.84×10 ⁻⁵
	5×10 ⁻⁷	34	1.06 (1.01-1.11)	7.15×10 ⁻³	54.74 (33)	0.01	40	1.12 (1.06-1.18)	3.22×10 ⁻⁵
	5×10 ⁻⁶	38	1.06 (1.01-1.10)	8.63×10 ⁻³	58.85 (37)	0.01	37	1.12 (1.06-1.18)	3.08×10 ⁻⁵

PD, Parkinson's disease; GWAS, genome-wide association studies; OR, odds ratio; CI, confidence interval; Q, Cochran's heterogeneity statistic;

Qdf, the degrees of freedom; *I*², 100%×(Q - Qdf)/Q [12]

Supplementary Table S7. Two-sample Mendelian randomization results of Parkinson's disease[1] (exposure trait) and schizophrenia[3] (outcome trait) using MR-Egger after removing outliers that exhibit pleiotropy detected by MR-PRESSO.

		MR-Egger			Heterogeneity (Egger)			Pleiotropy (Egger)	
		No. of SNPs	OR (95% CI)	<i>p</i>	Q (Qdf)	Q val	<i>I</i> ² (%)	Intercept OR (95% CI)	<i>p</i>
P threshold for PD GWAS	5×10 ⁻⁸	32	1.10 (1.00-1.21)	0.05	46.18 (30)	0.03	35	1.00 (0.98-1.01)	0.49
	5×10 ⁻⁷	34	1.12 (1.01-1.23)	0.03	54.20 (32)	0.01	41	0.99 (0.98-1.00)	0.26
	5×10 ⁻⁶	38	1.12 (1.02-1.23)	0.02	57.29 (36)	0.01	37	0.99 (0.98-1.00)	0.17

PD—Parkinson's disease; GWAS—genome-wide association studies; OR—odds ratio; CI—confidence interval; Q—Cochran's heterogeneity statistic; Qdf—the degrees of freedom; *I*²—100%×(Q - Qdf)/Q [12]

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