Supplementary

Table S1 *SNCA* (rs356219, rs11931074, rs356165) design-specific primers

Target site	Primer name	Primer sequence (5'→3')	Amplification length (bp)
SNCA rs356219	F1	TGCATGGGTATACTGGTGGTTCT	180
	R1	ACCCCTGCACCTTTCTTATTGC	
SNCA rs11931074	F1	GGGCCTGCACTAAAAGGGAA	157
	R1	GACAGTCAAATGGCAGCCTTC	
SNCA rs356165	F4	ACTGCCAGAAGTGTGTTTTG	410
	R4	TGTCTTATGGCTCTCTAAGGAG	

SNCA, synuclein alpha.

Table S2 PCR amplification process

Process	Temperature (℃)	Time	Cycle number
Predenaturation	98	4 min	1
Denaturation	98	10 s	40
Annealing	62	30 s	
Extend	72	40 s	
Extend	72	10 min	1
Maintain temperature	4	–	–

PCR, polymerase chain reaction.

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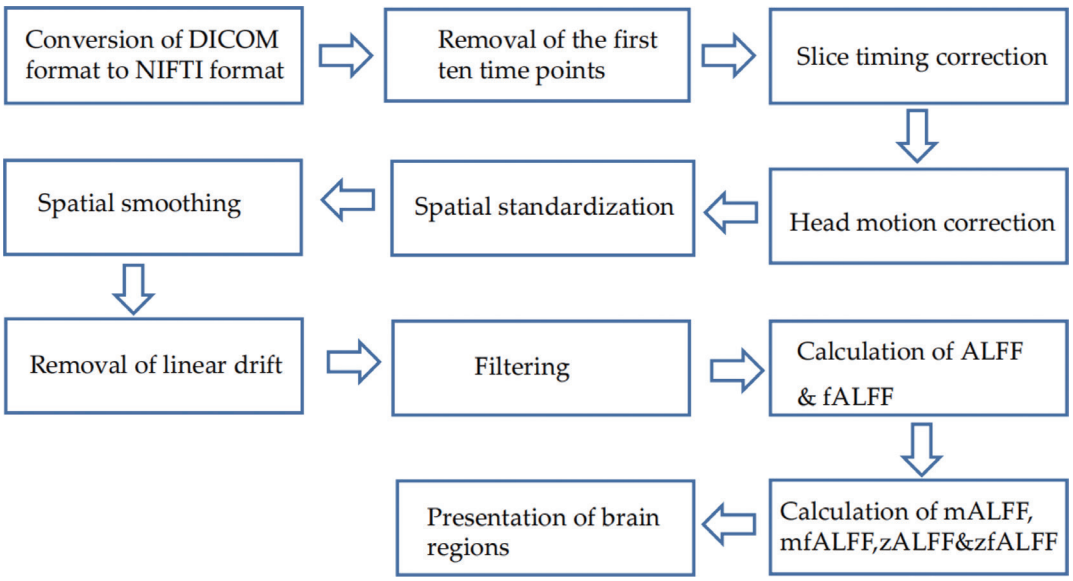

Figure S1 Flowchart of preprocessing for the rs-fMRI data. (I) Conversion of the DICOM format to NIFTI format through the dcm2niigui tool in MRIcron software. (II) Removal of the first 10 time points via CONN. The images of the first 10 time points were removed to eliminate the fluctuations in the BOLD value caused by the startup of the machine and the adaptation of the participants to the environment. (III) Slice timing was corrected to eliminate the phase difference of the scanning time of different slices. (IV) This study excluded participants whose head motion exceeded 2 mm in the x, y, and z direction and over 2° on the x-, y-, and z-axis. (V) For spatial standardization, the public EPI template was used to register the image of the participant to the standard brain space functional image template of the MNI and then resampled with a voxel size of 3×3×3 mm^3. (VI) Spatial smoothing was completed with a Gaussian kernel of 8×8×8 mm. (VII) Removal of linear drift was completed to further reduce the confounding signals caused by head movement, breathing, and heartbeat. (VIII) For filtering, the signals in the frequency range of 0.01–0.08 Hz were collected to analyze the spontaneous activities of brain neurons, and the effects of physiological noise were filtered out. (IX) The ALFF and fALFF calculation was completed with FFT as performed on the filtered time series to transform the time-domain signal to the frequency threshold to obtain the power spectrum using CONN. ALFF was calculated using the DPABI tool by taking the square root of the power spectrum. The amplitude of the current analysis frequency band was divided by the amplitude of the full frequency band to obtain the fALFF diagram. (X) The mALFF, zALFF, mfALFF, and zfALFF were calculated. For standardization purposes, the ALFF/fALFF value of each voxel was divided by the global mean ALFF value to obtain the mALFF/mfALFF value using the DPABI tool. In addition, Z transformation was performed, in which the deviation of the ALFF/fALFF value of each voxel was divided by the standard deviation of the whole brain ALFF/fALFF value in order to better align the data with a normal distribution and to obtain zALFF and zfALFF. (XI) An AAL brain atlas was used to mark the brain areas with significant differences in the ALFF values between different groups. The presentation of significant differences in brain regions was implemented using the Xjview 95 software. (XII) The rs-fMRI data were analyzed using SPM12 software (https://www.fil.ion.ucl.ac.uk/spm/software/SPM12). The comparison of the brain functional data in the PD and HC groups was performed by the two-sample *t*-test, with the covariates being age, sex, and MMSE. Multivariate regression analysis was used to calculate the correlation between the brain function data and MMSE score UPDRS III score, and disease course. Full factorial analysis was used to analyze the main effects of diseases and genotypes and their interaction effects on functional data, with the covariates being age and sex. The two-sample *t*-test was used to analyze the differences in functional data between G-allele carriers and non-G allele carriers, with the covariates being age, sex, and the MMSE score. rs-fMRI, resting-state functional magnetic resonance imaging; DICOM, Digital Imaging and Communications in Medicine; NIFTI, Neuroimaging Informatics Technology Initiative; CONN, Connectivity Toolbox; BOLD, blood oxygen level-dependent; EPI, echo planar imaging; MNI Montreal neurological institute; ALFF, amplitude of low-frequency fluctuation; fALFF, fractional amplitude of low frequency fluctuation; FFT, fast Fourier transform; DPABI, Data Processing & Analysis of Brain Imaging; mALFF, mean ALFF; zALFF, z-score ALFF; mfALFF, mean fALFF; zfALFF, z-score fALFF; AAL, automated anatomical labeling; PD, Parkinson's disease; HC, healthy control; MMSE, mini-mental state examination; UPDRS III, Unified Parkinson's Disease Rating Scale Part III.

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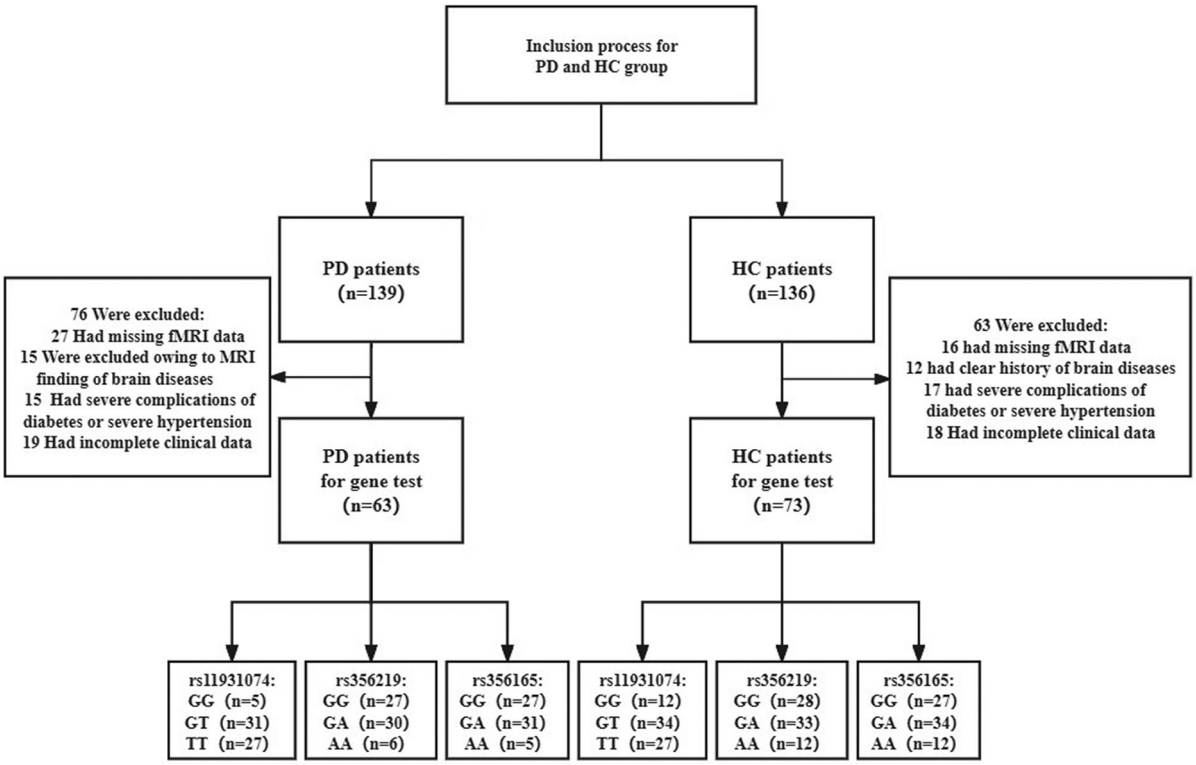

Figure S2. Flowchart of the inclusion process for the PD and HC groups. PD, Parkinson's disease; HC, healthy control; fMRI, functional magnetic resonance imaging; for rs11931074: GG, rs11931074 GG genotype; GT, rs11931074 GT genotype; TT, rs11931074 TT genotype; for rs356219: GG, rs356219 GG genotype; GA, rs356219 GA genotype; AA, rs356219 AA genotype; for rs356165: GG, rs356165 GG genotype; GA, rs356165 GA genotype; AA, rs356165 AA genotype.

Table S3 Hardy-Weinberg equilibrium of the rs11931074, rs356219, and rs356165 genotypes in the PD group and HC group

Group	GG	GT/GA	TT/AA	χ^2	P
rs11931074					
PD	5	31	27	0.92	0.63
HC	12	34	27	0.05	0.97
rs356219					
PD	27	30	6	0.32	0.85
HC	28	33	12	0.18	0.91
rs356165					
PD	27	31	5	0.92	0.63
HC	27	34	12	0.05	0.97

rs11931074 genotypes: GG, GT, and TT; rs356219, rs356165 genotypes: GG, GA, and AA. Results: P>0.05, the inheritance of the three gene loci in the PD group and the HC group was in accordance with the Hardy-Weinberg equilibrium, and the inheritance was consistent. PD, Parkinson's disease; HC, healthy control; for rs11931074: GG, rs11931074 GG genotype; GT, rs11931074 GT genotype; TT, rs11931074 TT genotype; for rs356219: GG, rs356219 GG genotype; GA, rs356219 GA genotype; AA, rs356219 AA genotype; for rs356165: GG, rs356165 GG genotype; GA, rs356165 GA genotype; AA, rs356165 AA genotype.

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Table S4 rs11931074, rs356219, and rs356165 linkage disequilibrium analysis

Polymorphic site	D'	r2
rs11931074-rs356219	0.984	0.968
rs11931074-rs356165	0.984	0.968
rs356219-rs356165	0.984	0.968

When the value of D 'and r2 is 0, the linkage is completely balanced; when the value of D' and r2 is 1, the linkage is completely unbalanced; the three loci are in line with the linkage disequilibrium.

Table S5 Comparison of the data of all participants and the rs11931074 G-allele carriers and non–G allele carriers in the PD group

Item	G-allele carrier	Non-G allele carriers	P
All participants			
Age (years)	63.70±7.09	62.26±7.69	0.266[a]
Gender: male/female	39/43	31/23	0.261[b]
Education (1/2/3/4/5)	9/18/24/21/10	4/12/13/18/7	0.428[f]
MMSE score	26.32±2.48	26.11±2.60	0.713[f]
PD group			
Age (years)	64.25±7.51	61.89±8.54	0.249[a]
Gender: male/female	21/15	16/11	0.941[c]
MMSE score	24.83±2.60	24.96±3.01	0.855[a]
UPDRS III score	28.36±10.64	33.74±11.71	0.062[a]
Course of disease (months)	47.14±30.98	64.33±52.19	0.300[f]
Hoehn-Yahr stage	2.26±0.52	2.44±0.64	0.547[f]
Education (1/2/3/4/5)	7/9/8/8/4	3/7/4/9/4	0.768[d]
LEDD, mg/day	349.26±216.50	414.57±259.67	0.259[g]

Data are shown as the mean ± standard deviation or number. [a], two-sample *t*-test; [b], Pearson Chi-square test; [c], Kruskal-Wallis test; [d], Fisher exact probability method; [e], ANOVA; [f], Mann-Whitney test; [g], Wilcoxon test. 1, illiterate; 2, elementary school; 3, junior high school; 4, high school/technical secondary school; 5, university/college. PD, Parkinson's disease; MMSE, mini-mental state examination, UPDRS III, Unified Parkinson's Disease Rating Scale Part III; ANOVA, analysis of variance.

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Table S6 Significant differences in ALFF value between the PD group and HC group

Item	Brain area (AAL template)	Clump size (voxel)	Peak point (*t* value)	Peak point MNI coordinate		
				X	Y	Z
mALFF HC-PD	Cerebelum_Crus1_R	79	4.6407	18	−75	−33
	Vermis_7	77	4.8223	0	−78	−21
	Supp_Motor_Area_L	39	4.3848	−12	6	69
zALFF HC-PD	Cerebelum_Crus1_R	71	4.5467	18	−75	−33
	Vermis_7	69	4.6799	0	−78	−21
	Supp_Motor_Area_L	36	4.3177	−12	6	69

ALFF, amplitude of low-frequency fluctuation; PD, Parkinson's disease; HC, healthy control; AAL, anatomical automatic labeling; MNI, Montreal neurological institute; mALFF, mean amplitude of low-frequency fluctuation; R, right; L, left; zALFF, z-score amplitude of low-frequency fluctuation; Cerebelum_Crus1_R, the right superior cerebellum; Vermis_7, vermis; Supp_Motor_Area_L, left supplementary motor area.

Table S7 The correlation of brain functional data in PD group and HC group with clinical scale and disease course

Item	Brain area (AAL template)	Clump size (voxel)	Peak point (*t* value)	Peak point MNI coordinate			r_s	P
				X	Y	Z		
PD zALFF & MMSE	Postcentral_L	46	4.2641	−57	−3	12	0.542	<0.001*
HC mfALFF & MMSE	SupraMarginal_R	36	−4.7196	57	−42	30	−0.528	<0.001*
PD zALFF & course	Cerebelum_Crus2_R	46	5.9361	12	−93	−39	0.194	0.129
	Hippocampus_R	43	6.0211	30	−6	−18	0.194	0.129
	Frontal_Sup_Orb_R	38	5.0201	30	66	−3	0.311	0.013*
	Parietal_Sup_R	53	4.3902	27	−51	66	0.189	0.138

*, P<0.05, significant difference. PD, Parkinson's disease; HC, healthy control; AAL, anatomical automatic labeling; MNI, Montreal neurological institute; R, right; L, left; zALFF, z-score amplitude of low-frequency fluctuation; mfALFF, mean fractional amplitude of low-frequency fluctuation; Postcentral_L, left posterior central gyrus; SupraMarginal_R, right supramarginal gyrus; Cerebelum_Crus2_R, right inferior cerebellum; Hippocampus_R, right hippocampus; Frontal_Sup_Orb_R, right superior frontal gyrus, orbital part; Parietal_Sup_R, right superior parietal gyrus.

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Table S8 Comparison of brain function indexes between the rs11931074 genotype groups and the main effect brain regions of genes

Item	Brain area (AAL template)	Clump size (voxel)	Peak point (*F*/*t* value)	Peak point MNI coordinate		
				X	Y	Z
Full factorial (main effect of genotypes)						
mALFF	Cerebelum_9_L	228	23.6754*	–9	–54	–54
mfALFF	Cingulum_Ant_R	61	23.4456*	3	30	9
zALFF	Cerebelum_9_L	131	22.1504*	–9	–54	–54
zfALFF	Cingulum_Ant_R	62	24.4574*	3	30	9
Two-sample *t*-test (PD + HC)						
mfALFF	Caudate_L	51	3.1536*	–3	15	3
zfALFF	Caudate_L	67	3.1536*	–3	15	3
Two-sample *t*-test (PD)						
mfALFF	Postcentral_R	51	3.2368*	51	–30	54
zfALFF	Postcentral_R	51	3.2368*	51	–30	54

*, P<0.05, significant difference. AAL, anatomical automatic labeling; MNI, Montreal neurological institute; R, right; L, left; PD, Parkinson's disease; HC, healthy control; ALFF, amplitude of low-frequency fluctuation; mALFF, mean amplitude of low-frequency fluctuation; zALFF, z-score amplitude of low-frequency fluctuation; mfALFF, mean fractional amplitude of low-frequency fluctuation; zfALFF, z-score fractional amplitude of low-frequency fluctuation; Cerebelum_9_L, left inferior cerebelum; Cingulum_Ant_R, right anterior cingulate and paracingulate gyri; Caudate_L, left caudate nucleus; Postcentral_R, right postcentral gyrus.

Table S9 Comparison of brain function indexes between the rs356219 genotype groups and a full factor analysis of significant brain areas

Item	Brain area (AAL template)	Clump size (voxel)	Peak point (*F*/*t* value)	Peak point MNI coordinate		
				X	Y	Z
Full factorial (main effect of genotypes)						
mfALFF	Caudate_L	49	21.6771*	–3	15	0
Groups × genotype interaction						
zfALFF	Parietal_Inf_R	44	25.2145*	54	–33	57

*, P<0.05 significant difference. AAL, anatomical automatic labeling; MNI, Montreal neurological institute; R, right; L, left; PD, Parkinson's disease; HC, healthy control; mfALFF, mean fractional amplitude of low-frequency fluctuation; zfALFF, z-score fractional amplitude of low-frequency fluctuation; Caudate_L, left caudate nucleus; Parietal_Inf_R, right inferior parietal gyrus.

Table S10 Comparison of brain function indexes in each genotype group of rs356165 and the significant brain areas of the gene main cause effects

Item	Brain area (AAL template)	Clump size (voxel)	Peak point (*F*/*t* value)	Peak point MNI coordinate		
				X	Y	Z
Full factorial (main effect of genotypes)						
mfALFF	Caudate_L	73	24.1354*	–6	18	0
zfALFF	Caudate_L	73	19.3663*	–3	15	0

*, P<0.05, significant difference. AAL, anatomical automatic labeling; MNI, Montreal neurological institute; R, right; L, left; PD, Parkinson's disease; HC, healthy control; mfALFF, mean fractional amplitude of low-frequency fluctuation; zfALFF, z-score fractional amplitude of low-frequency fluctuation; Caudate_L, left caudate nucleus.

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