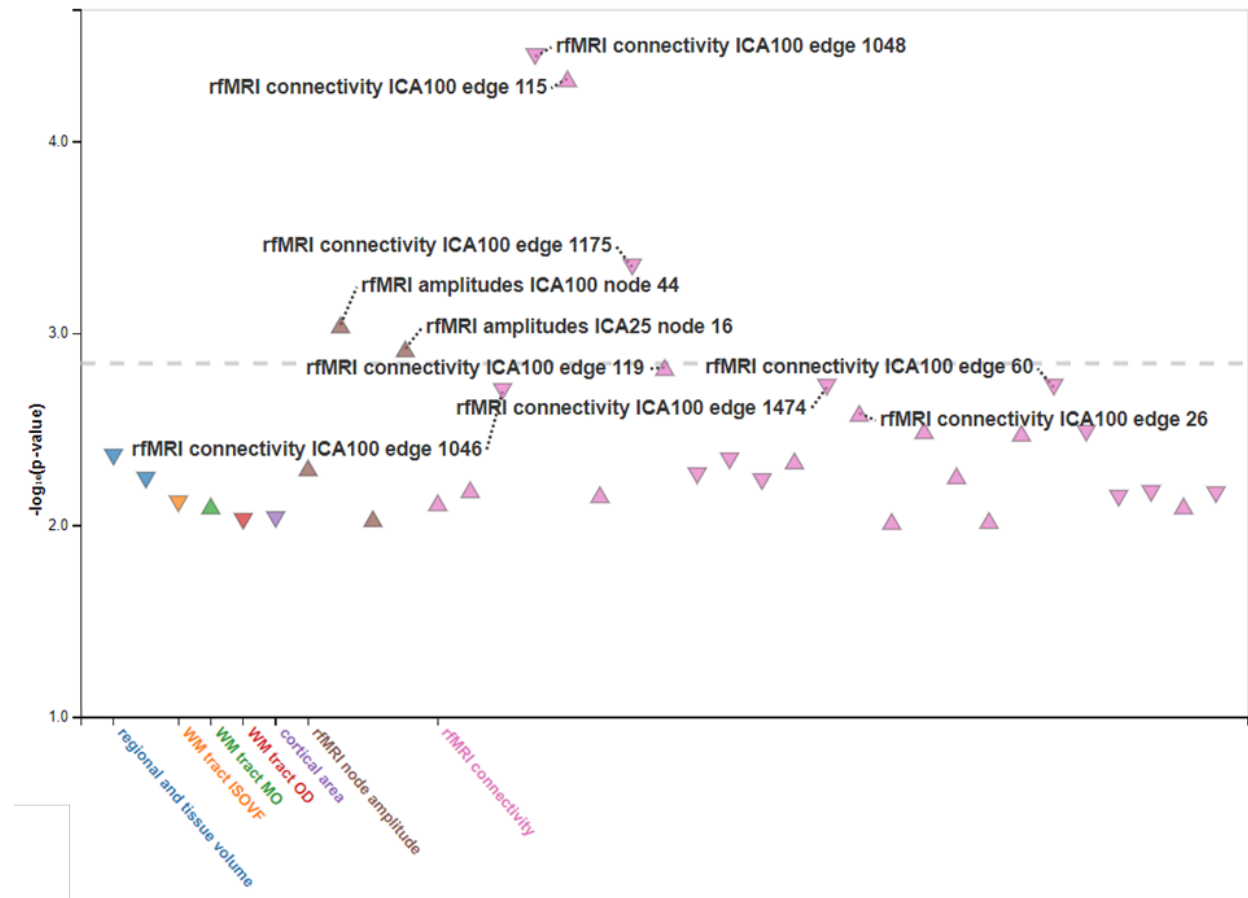# Supplementary Material

Parkinson's Disease Risk Variant rs9638616 is Non-Specifically Associated with Altered Brain Structure and Function

Supplementary Figure 1. Phenome-wide association analysis for rs9638616 in UK Biobank.

Supplementary Material 1. Post-hoc power calculations for comparable studies

Known studies of PD were included in Supplementary Table 2 if they compared an imaging measure between risk variant carriers and non-carriers. We then converted test statistics to effect sizes and estimated the achieved power for our study's sample size when a similar effect size is applied. Statistical power was calculated using G*Power 3.1.9.6 for an independent-samples two-tailed t-test with alpha=0.05. For each study, only the largest and smallest reported effects were included in Supplementary Table 1.
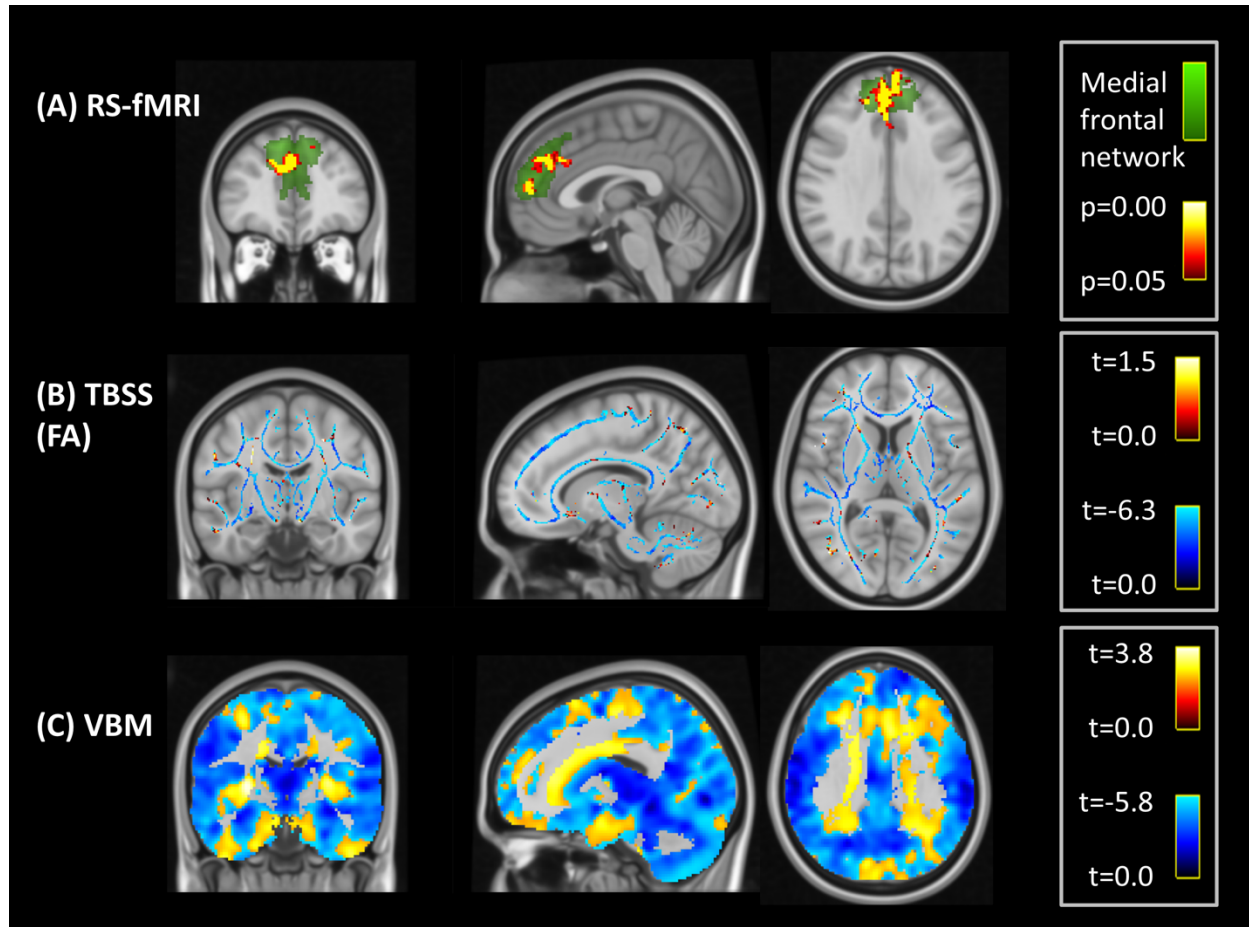
Supplementary Table 1.

Study	Phenotype	Test statistic	Effect size	Achieved power in our study, assuming the same effect size
[1]	Grey matter volume within clusters	t=4.26 t=-4.71	1.27 [a] -1.40 [a]	>90% >90%
[2]	Degree centrality of brain regions based on structural connectivity	t=-2.46 [b] t=-2.00 [b]	-0.46 [a] -0.37 [a]	78% 60%
[3]	Degree centrality of brain regions based on structural connectivity	t=-3.90 [b] t=-2.35 [b]	-0.87 [a] -0.53 [a]	>90% 88%
[4]	Task fMRI activation in putamen and motor cortex	t=2.60 t=2.27	0.94 [c] 0.83 [c]	>90% >90%
[5]	Amplitude of low-frequency fluctuations in fusiform gyrus	t=-4.59	-0.77 [a]	>90%

[a]Cohen's d estimated from t-value and sample size using Pustejovsky's method [6]; [b]From t-distribution lookup table based on reported p-values and sample sizes; [c]Hedge's g.

Supplementary Material 2. PD vs. control group comparisons (irrespective of rs9638616 genotype).

We performed PD versus control group comparisons for each of our imaging modalities (VBM for grey matter volumetry, TBSS for white matter tract FA, and MELODIC dual regression for fMRI resting-state networks). Each comparison used the same set of regressors (age, sex, education, and white matter hyperintensity burden).

For VBM and TBSS, the voxelwise PD vs. control group comparisons were non-significant but the parametric maps did reveal symmetrical patterns suggesting biologically feasible yet sub-threshold differences, which were concordant with PD-associated imaging findings from the literature. For fMRI, there was a significant group difference detected in one cluster in the frontal lobe, belonging to the medial frontal lobe resting-state network. After correcting for the number of networks tested, this was also non-significant.

Supplementary Figure 2. Group comparisons of PD and control groups. A) One large significant cluster was detected indicating lower functional connectivity of the medial frontal cortex in the PD group with the medial frontal resting-state fMRI network (green). B) Tract FA was generally lower in PD than controls (blue voxels), but did not reach significance. C) Symmetrical patterns of grey matter volume change were observed showing mostly reduced volume in the cortex in PD, but were also non-significant.

Supplementary Table 2. Comparisons of study variables between rs9638616 carriers and non-carriers.

	t	p
Age	1.310	0.192
Sex	0.012	0.991
Disease duration	-1.520	0.131
MMSE	0.519	0.604
MoCA	0.652	0.515
Digit span	0.116	0.908
MDS-UPDRS-III (Baseline)	-0.660	0.510
H&Y Stage (Baseline)	-1.093	0.276
MDS-UPDRS-III Baseline-to-3-Year Difference	0.830	0.408
MDS-UPDRS-III Baseline-to-5-Year Difference	0.174	0.862
H&Y Stage Baseline-to-3-Year Difference	0.739	0.461
H&Y Stage Baseline-to-5-Year Difference	-0.242	0.811

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