Supplementary material

1. Results of statistical analyses for all ROIs

Results of the statistical tests in all eight regions in the SIME analysis, for V_{ND}, V_T and V_S can be found in the following tables. Table 1 shows the results of the paired-sample t-test for the lipopolysaccharide dataset. ANOVA results are displayed in Table 2 for alcohol use disorder, in Table 3 for first-episode psychosis, and in Table 4 for Parkinson's disease.

Table 1: Results of the paired-sample t-test for the lipopolysaccharide (LPS) dataset

	P(LPS)		
	V_{ND}	**V_T**	**V_S**
Caudate	0.38	0.0034	0.0014
Cerebellum		0.016	0.0052
Frontal cortex		0.0012	2.6E-4
Occipital cortex		0.036	0.044
Parietal cortex		0.047	0.055
Putamen		0.0015	6.4E-4
Temporal cortex		0.0067	0.0075
Thalamus		0.022	0.022

*Table 2: Results of the ANOVA for the alcohol use disorder dataset. * One subject removed due to fitting failure of the two-tissue compartment model.*

	P(diagnosis)			**P(genotype)**		
	V_{ND}	**V_T**	**V_S**	**V_{ND}**	**V_T**	**V_S**
Caudate	8.4E-4	0.089	0.85	0.36	0.0032	1.4E-4
Cerebellum		0.012	0.15		2.3E-6	5.7E-8
Frontal cortex		0.0048	0.065		4.4E-4	8.0E-5
Occipital cortex*		0.011	0.11		4.5E-4	4.9E-5
Parietal cortex		0.022	0.31		2.7E-5	2.6E-6
Putamen		0.085	0.89		1.2E-5	9.3E-7
Temporal cortex		0.023	0.36		1.8E-5	9.9E-7
Thalamus		0.081	0.57		2.0E-5	1.1E-6

Table 3: Results of the ANOVA for the first episode psychosis dataset

	P(diagnosis)			**P(genotype)**		
	V_{ND}	**V_T**	**V_S**	**V_{ND}**	**V_T**	**V_S**
Caudate	0.30	0.047	0.030	0.0043	0.022	0.17
Cerebellum		0.060	0.054		0.011	0.073
Frontal cortex		0.045	0.033		0.017	0.099
Occipital cortex		0.050	0.051		0.0094	0.057
Parietal cortex		0.034	0.023		0.012	0.066
Putamen		0.050	0.033		0.0061	0.023
Temporal cortex		0.060	0.049		0.0071	0.044
Thalamus		0.042	0.029		0.0071	0.018

Table 4: Results of the ANOVA for the Parkinson's disease dataset

	P(diagnosis)			**P(genotype)**		
	V_{ND}	**V_T**	**V_S**	**V_{ND}**	**V_T**	**V_S**
Caudate	0.0032	0.15	0.47	0.012	3.7E-7	2.9E-6
Cerebellum		0.78	0.17		4.3E-8	6.7E-7
Frontal cortex		0.36	0.38		6.9E-9	8.5E-9
Occipital cortex		0.73	0.12		1.1E-8	2.2E-8
Parietal cortex		0.50	0.21		1.2E-8	2.1E-8
Putamen		0.35	0.48		3.1E-7	9.1E-7
Temporal cortex		0.59	0.17		7.0E-9	1.9E-8
Thalamus		0.78	0.25		5.4E-9	1.5E-9

2. ANOVA with diagnosis*genotype interaction

In the following tables the results of an ANOVA which includes a diagnosis*genotype interaction term are presented; in Table 5 for alcohol use disorder, in Table 6 for first-episode psychosis, and in Table 7 for Parkinson's disease.

Table 5: Results of ANOVA with an interaction term for the alcohol use disorder dataset

	P(diagnosis)			**P(genotype)**			**P(diagnosis*genotype)**		
	V_{ND}	**V_T**	**V_S**	**V_{ND}**	**V_T**	**V_S**	**V_{ND}**	**V_T**	**V_S**
Caudate	8.4E-4			0.33			0.18		
Cerebellum		0.014	0.15		3.5E-6	9.3E-8		0.86	0.64
Frontal cortex		0.0048	0.058		4.5E-4	6.8E-5		0.38	0.21
Occipital cortex		0.011	0.097		4.7E-4	4.4E-5		0.42	0.24
Parietal cortex		0.025	0.32		3.9E-5	4.1E-6		0.89	0.99
Putamen		0.093	0.90		1.8E-5	1.5E-6		0.78	0.80
Temporal cortex		0.026	0.37		2.6E-5	1.6E-6		0.89	0.95
Thalamus		0.088	0.59		2.7E-5	1.5E-6		0.47	0.44

*Table 6: Results of ANOVA with an interaction term for the first episode psychosis dataset. * one subject excluded du to fitting failure of the two-tissue compartment model.*

	P(diagnosis)			**P(genotype)**			**P(diagnosis*genotype)**		
	V_{ND}	**V_T**	**V_S**	**V_{ND}**	**V_T**	**V_S**	**V_{ND}**	**V_T**	**V_S**
Caudate	0.26	0.018	0.011	0.0043	0.013	0.14	0.20	0.0069	0.0089
Cerebellum		0.024	0.020		0.0061	0.052		0.0073	0.0059
Frontal cortex		0.019	0.014		0.011	0.083		0.011	0.015
Occipital cortex *		0.025	0.023		0.0064	0.046		0.013	0.0089
Parietal cortex		0.016	0.011		0.0081	0.056		0.019	0.026
Putamen		0.023	0.014		0.0037	0.016		0.016	0.015
Temporal cortex		0.025	0.019		0.0038	0.030		0.0085	0.0070
Thalamus		0.020	0.013		0.0046	0.013		0.021	0.019

Table 7: Results of ANOVA with an interaction term for the Parkinson's disease dataset

	P(diagnosis)			**P(genotype)**			**P(diagnosis*genotype)**		
	V_{ND}	**V_T**	**V_S**	**V_{ND}**	**V_T**	**V_S**	**V_{ND}**	**V_T**	**V_S**
Caudate		0.16	0.48		5.8E-7	4.2E-6		0.81	0.91
Cerebellum		0.78	0.16		4.5E-8	5.4E-7		0.23	0.14
Frontal cortex		0.37	0.38		1.2E-8	1.4E-8		0.70	0.53
Occipital cortex	0.0036	0.73	0.13	0.013	1.8E-8	3.0E-8	0.57	0.63	0.41
Parietal cortex		0.51	0.22		2.2E-8	3.5E-8		0.92	0.74
Putamen		0.35	0.47		3.7E-7	7.3E-7		0.32	0.14
Temporal cortex		0.59	0.17		1.0E-8	2.3E-8		0.46	0.27
Thalamus		0.78	0.25		8.8E-9	2.2E-9		0.54	0.40

3. Results for SIME with ROI weights

The following tables presents the results of the statistical testing when SIME V_{ND} was estimated using size-based ROI weights. The contribution of each ROI was weighted by the ratio of the region volume to the volume of the largest included region. The results for LPS are presented in Table 9, for alcohol use disorder in Table 10, for first-episode psychosis in Table 11, and for Parkinson's Disease in Table 12.

Table 8: Results of a pair-sample t-test on the lipopolysaccharide (LPS) dataset, where SIME V_{ND} was estimated with size-based ROI weights

	P(LPS)	
	V_{ND}	**V_S**
Caudate	0.41	0.0011
Cerebellum		0.0050
Frontal cortex		2.3E-4
Occipital cortex		0.043
Parietal cortex		0.054
Putamen		7.0E-4
Temporal cortex		0.0076
Thalamus		0.026

Table 9: Results of the ANOVA on the alcohol use disorder dataset, where SIME V_{ND} was estimated using size-based ROI weights.

	P(diagnosis)		**P(genotype)**	
	V_{ND}	**V_S**	**V_{ND}**	**V_S**
Caudate	0.0010	0.86	0.20	1.4E-4
Cerebellum		0.15		6.3E-8
Frontal cortex		0.068		6.3E-5
Occipital cortex		0.11		3.7E-5
Parietal cortex		0.31		2.0E-6
Putamen		0.93		1.6E-6
Temporal cortex		0.38		1.2E-6
Thalamus		0.60		1.2E-6

Table 10: Results of the ANOVA on the first episode psychosis dataset, where SIME V_{ND} was estimated using size-based ROI weights

	P(diagnosis)		**P(genotype)**	
	V_{ND}	**V_S**	**V_{ND}**	**V_S**
Caudate	0.33	0.031	0.0045	0.15
Cerebellum		0.050		0.065
Frontal cortex		0.031		0.090
Occipital cortex		0.047		0.050
Parietal cortex		0.022		0.059
Putamen		0.033		0.022
Temporal cortex		0.046		0.039
Thalamus		0.029		0.017

Table 11: Results of the ANOVA on the Parkinson's disease dataset, where SIME V_{ND} was estimated using size-based ROI weights

	P(diagnosis)		**P(genotype)**	
	V_{ND}	**V_S**	**V_{ND}**	**V_S**
Caudate	0.0014	0.47	0.017	2.9E-6
Cerebellum		0.17		6.7E-7
Frontal cortex		0.38		8.5E-9
Occipital cortex		0.12		2.2E-8
Parietal cortex		0.21		2.1E-8
Putamen		0.48		9.1E-7
Temporal cortex		0.17		1.9E-8
Thalamus		0.25		1.5E-9

4. ANOVA for V_{ND} with gray matter volume as covariate

Table 5 holds the results for V_{ND} of an ANOVA which includes gray matter volume as a covariate.

Table 12: Results for ANOVA on V_{ND} with gray matter volume as covariate, for the alcohol use disorder, first episode psychosis and Parkinson's disease datasets

Dataset	**P(diagnosis)**	**P(genotype)**	**P(volume)**
Alcohol use disorder	0.0026	0.52	0.53
First episode psychosis	0.30	0.0053	0.38
Parkinson’s disease	0.0039	0.038	0.63

5. Results for SIME executed on a larger ROI set

For the two datasets from Karolinska Institutet we additionally calculated V_{ND} using a larger ROI set than the one presented in the manuscript. These ROIs were frontal cortex, temporal cortex, parietal cortex, occipital cortex, limbic lobe, striatum, thalamus, insula, anterior cingulate cortex, posterior cingulate cortex, and cerebellum. The results of the ANOVA for these V_{ND} values are presented in Table 13.

Table 13: Results of the ANOVA for V_{ND} calculated on a larger ROI set

Dataset	**P(diagnosis)**	**P(genotype)**
First episode psychosis	0.35	0.0074
Parkinson's disease	0.0023	0.010