

Supplementary Materials

Brain-clinical biotyping in patients with idiopathic REM sleep behavior disorder

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Fig. S2. Functional connectivity differences between Biotype 1 and the control group using Desikan-Killiany and aseg atlas.

Table S1. Model variables by data type.

Data Type	Variables
Cortical Thickness	Thickness (mm) measures (bilateral): - Banks of the superior temporal sulcus - Cuneus - Entorhinal - Frontal pole - Fusiform gyrus - Inferior and superior parietal gyrus - Inferior and superior temporal gyrus - Insula - Lateral occipital gyrus - Lateral and medial orbitofrontal gyrus - Lingual gyrus - Paracentral gyrus - Parahippocampal gyrus - Pars opercularis, pars triangularis, and pars orbitalis - Pericalcarine - Postcentral gyrus - Precentral gyrus - Precuneus - Rostral and caudal middle frontal gyrus - Rostral anterior, caudal anterior, posterior and isthmus of the cingulate - Superior, middle and inferior temporal gyrus - Supramarginal gyrus - Temporal pole - Transverse temporal gyrus
Surface area	Area (mm²) measures (bilateral): - Banks of the superior temporal sulcus - Cuneus - Entorhinal - Frontal pole - Fusiform gyrus - Inferior and superior parietal gyrus - Inferior and superior temporal gyrus - Insula - Lateral occipital gyrus - Lateral and medial orbitofrontal gyrus - Lingual gyrus - Paracentral gyrus

	- Parahippocampal gyrus - Pars opercularis, pars triangularis, and pars orbitalis - Pericalcarine - Postcentral gyrus - Precentral gyrus - Precuneus - Rostral and caudal middle frontal gyrus - Rostral anterior, caudal anterior, posterior and isthmus of the cingulate - Superior, middle and inferior temporal gyrus - Supramarginal gyrus - Temporal pole - Transverse temporal gyrus
Subcortical Volumes	Volumes (mm³): - Bilateral cerebellum - Bilateral thalamus - Bilateral caudate - Bilateral putamen - Bilateral pallidum - Bilateral hippocampus - Bilateral amygdala - Bilateral accumbens - Bilateral ventral DC - Brainstem - CC_Posterior - CC_Mid_Posterior - CC_Central - CC_Mid_Anterior - CC_Anterior
Clinical assessments	- RBDQ-HK-factor1 - RBDQ-HK-factor2 - HADS-D - HADS-A - MoCA (10 items) - UPDRS-III (27items)

Abbreviations: CC, cingulate cortex; RBDQ-HK, Rapid eye movement sleep behavior disorder questionnaire-Hong Kong; HADS-D/A, Hospital Anxiety and Depression Scale-Depression/Anxiety score; MoCA, Montreal Cognitive Assessment; UPDRS, Unified Parkinson's Disease Rating Scale.

Table S2. Clinical and neurogenerative markers of iRBD biotypes and controls.

	Biotype 1 ¹	Biotype 2 ²	Control ³	<i>p</i> value ^{&}	Post-hoc [@]
TIV, mm ³ , mean (SD)	1.51 (0.13) ×10 ⁶	1.50 (0.13) ×10 ⁶	1.46 (0.15) ×10 ⁶	0.016	1=2, 1>3, 2=3
Handedness, left (%)	2 (2.3%)	2 (3.5%)	3 (2.4%)	0.86	-
MoCA-HK, subscale score, mean (SD)					
Executive and visuospatial function	4.00 (0.87)	4.28 (0.85)	4.27 (0.76)	0.03	-
Naming	2.89 (0.34)	2.94 (0.23)	2.87 (0.35)	0.36	-
Attention	5.29 (0.88)	5.51 (0.98)	5.41 (1.19)	0.39	-
Language	2.93 (0.26)	2.92 (0.38)	2.86 (0.56)	0.51	-
Abstraction	1.23 (0.76)	1.34 (0.78)	1.37 (0.68)	0.40	-
Delayed recall	2.76 (1.49)	3.21 (1.6)	3.56 (1.23)	<0.001	1=2, 1<3, 2=3
Orientation	5.89 (0.34)	5.84 (0.36)	5.92 (0.28)	0.30	-
UPDRS-III, subscale score, mean (SD)					
Tremor	1.16 (1.41)	0.67 (1.20)	0.23 (0.70)	<0.001	1>2>3
Rigidity	1.24 (2.42)	0.60 (1.46)	0.10 (0.40)	<0.001	1>2=3
Bradykinesia	3.51 (3.66)	1.59 (2.88)	0.82 (1.80)	<0.001	1>2=3
HADS, subscale score, mean (SD)					
Depression score	5.60 (3.69)	5.91 (3.86)	4.16 (3.25)	0.007	1=2>3
Anxiety score	4.87 (3.63)	5.87 (3.90)	3.68 (3.16)	0.002	1=2>3
Neurodegenerative risk factors and biomarkers					
Regular pesticide exposure, n (%)	1 (1.56)	2 (2.86)	4 (4.88)	0.52	-
Nonuse of caffeine n (%)	34 (43.59)	32 (39.02)	41 (37.27)	0.68	-
Nonsmoking, n (%)	53 (62.35)	68 (79.07)	113 (90.4)	<0.001	1<2=3
First-degree relatives with neurogenerative disease, n (%)					
PD	5 (6.49)	9 (11.69)	0	0.002	1=2>3
Dementia	8 (10.39)	14 (17.95)	0	<0.001	1=2>3

Diabetes mellitus (type II), n (%)	8 (13.79)	8 (14.04)	14 (19.44)	0.61	-
Subthreshold parkinsonism, n (%)	51 (59.3)	26 (30.59)	19 (15.57)	<0.001	1>2>3
Olfactory loss, n (%)	56 (72.73)	48 (61.54)	17 (14.91)	<0.001	1=2>3
Constipation, n (%)	43 (51.19)	34 (40.48)	7 (6.03)	<0.001	1=2>3
Erectile dysfunction, Male only, n (%)	22 (42.31)	12 (24.49)	7 (13.46)	0.004	1=2, 1>3, 2=3
Urinary dysfunction, n (%)	6 (7.5)	8 (10)	6 (5.77)	0.56	-
Orthostatic Blood Pressure drop, mmHg, mean (SD)					
Systolic Blood Pressure drop	5.46 (14.27)	0.75 (13.36)	-2.45 (10.92)	0.001	1=2, 1>3, 2=3
Diastolic Blood Pressure drop	-0.57 (8.83)	-2.28 (7.27)	-4.49 (7.48)	0.007	1=2, 1>3, 2=3
Physical activity					
Strenuous exercise, hrs per week	90.13 (294.53)	50.96 (135.64)	60.16 (165.59)	0.43	-
Moderate exercise, hrs per week	115.83 (168.02)	140.18 (253.65)	121.37 (187.09)	0.72	-
Mild exercise, hrs per week	336.68 (427.15)	355.52 (514.48)	294.58 (391.80)	0.59	-
Long-term (3-months) medications history					
Melatonin only, n (%)	6 (11.53)	4 (7.27)	-	0.45	-
Clonazepam only, n (%)	15 (28.85)	14 (25.45)	-	0.69	-
Melatonin + Clonazepam, n (%)	12 (23.08)	6 (10.91)	-	0.09	-

&p value was calculated with one-way ANOVA, ANCOVA or chi-square test.

@Bonferroni correction was applied to adjust for multiple comparisons of post-hoc analyses, significance was thresholded at $p < 0.017$.

Abbreviation: iRBD, isolated Rapid eye movement sleep behavior disorder; TIV, total intracranial volume; MoCA, Montreal Cognitive Assessment; UPDRS, Unified Parkinson's Disease Rating Scale; HADS, Hospital Anxiety and Depression Scale; SCOPA-AUT, Scales for Outcomes in Parkinson's Disease-Autonomic; OIT, Olfactory Identification Test; MDS, Movement Disorder Society; LR, Likelihood ratio; PD, Parkinson's disease.

Table S3. Cortical thickness of cortical regions in Biotype 1, Biotype 2 and control.

Label	Left hemisphere (mean, mm)					Right hemisphere (mean, mm)				
	Biotype 1	Biotype 2	Control	p value ^{&}	Post-hoc [@]	Biotype 1	Biotype 2	Control	p value ^{&}	Post-hoc [@]
Banks STS	2.37	2.35	2.37	0.418	-	2.44	2.35	2.45	0.47	-
Caudal anterior cingulate	2.48	2.42	2.46	0.274	-	2.35	2.42	2.35	0.609	-
Caudal middle frontal	2.53	2.51	2.53	0.292	-	2.50	2.51	2.50	0.532	-
Cuneus	1.74	1.73	1.72	0.691	-	1.82	1.73	1.81	0.349	-
Entorhinal	3.20	3.23	3.27	0.416	-	3.35	3.23	3.37	0.949	-
Fusiform	2.63	2.63	2.64	0.953	-	2.65	2.63	2.65	0.882	-
Inferior parietal	2.32	2.34	2.36	0.737	-	2.35	2.34	2.37	0.823	-
Inferior temporal	2.71	2.71	2.74	0.222	-	2.73	2.71	2.78	0.045	-
Isthmus cingulate	2.22	2.20	2.24	0.099	-	2.19	2.20	2.22	0.149	-
Lateral occipital	2.07	2.06	2.06	0.407	-	2.12	2.06	2.12	0.63	-
Lateral orbitofrontal	2.56	2.52	2.55	0.053	-	2.61	2.52	2.59	0.13	-
Lingual	1.84	1.83	1.83	0.916	-	1.88	1.83	1.87	0.813	-
Medial orbitofrontal	2.40	2.38	2.41	0.172	-	2.43	2.38	2.45	0.003	-
Middle temporal	2.73	2.73	2.76	0.218	-	2.74	2.73	2.77	0.517	-
Parahippocampal	2.43	2.47	2.44	0.526	-	2.39	2.47	2.44	0.337	-
Paracentral	2.43	2.43	2.41	0.203	-	2.46	2.43	2.46	0.186	-
Pars opercularis	2.51	2.50	2.51	0.425	-	2.53	2.50	2.52	0.504	-
Pars orbitalis	2.64	2.61	2.63	0.444	-	2.67	2.61	2.66	0.303	-
Pars triangularis	2.35	2.36	2.37	0.944	-	2.40	2.36	2.39	0.175	-
Pericalcarine	1.50	1.46	1.46	0.036	-	1.54	1.46	1.51	0.11	-
Postcentral	2.03	2.03	2.04	0.469	-	2.03	2.03	2.03	0.68	-
Posterior cingulate	2.37	2.33	2.37	0.097	-	2.35	2.33	2.36	0.932	-
Precentral	2.52	2.54	2.53	0.81	-	2.45	2.54	2.46	0.062	-
Precuneus	2.25	2.27	2.28	0.761	-	2.27	2.27	2.29	0.76	-
Rostral anterior cingulate	2.66	2.64	2.68	0.494	-	2.71	2.64	2.68	0.784	-
Rostral middle frontal	2.37	2.34	2.36	0.188	-	2.39	2.34	2.37	0.161	-
Superior frontal	2.72	2.70	2.72	0.271	-	2.70	2.70	2.71	0.416	-
Superior parietal	2.12	2.12	2.13	0.726	-	2.08	2.12	2.10	0.74	-
Superior temporal	2.59	2.61	2.63	0.786	-	2.63	2.61	2.66	0.932	-
Supramarginal	2.42	2.44	2.44	0.761	-	2.41	2.44	2.44	0.969	-
Frontal pole	2.74	2.69	2.72	0.189	-	2.75	2.69	2.75	0.153	-
Temporal pole	3.50	3.52	3.55	0.854	-	3.57	3.52	3.65	0.18	-
Transverse temporal	2.25	2.21	2.22	0.245	-	2.26	2.21	2.25	0.307	-
Insula	2.87	2.87	2.87	0.948	-	2.88	2.87	2.92	0.229	-

[&]p value was calculated with one-way ANOVA, and Bonferroni correction was applied to adjust for multiple comparisons of 34 regions on each hemisphere, a $p \leq 0.001$ is considered statistical significance.

[@]Bonferroni correction was applied to adjust for multiple comparisons of three groups, significance was thresholded at $p < 0.017$.

Table S4. Surface area of cortical regions in Biotype1, Biotype 2 and control.

Label	Left hemisphere (mean, mm ²)					Right hemisphere (mean, mm ²)				
	Biotype1	Biotype2	Control	p value ^{&}	Post-hoc [@]	Biotype1	Biotype2	Control	p value ^{&}	Post-hoc [@]
Banks STS	879.10	917.43	890.74	0.107	-	773.74	814.66	798.80	0.033	-
Caudal anterior cingulate	541.45	554.43	550.82	0.412	-	669.35	720.05	675.90	0.021	-
Caudal middle frontal	1877.47	2013.90	1994.77	<0.001	1<2=3	1764.30	1870.71	1877.60	<0.001	1<2=3
Cuneus	1443.45	1543.23	1487.89	0.001	1<2=3	1530.43	1615.73	1546.03	0.006	-
Entorhinal	391.71	436.17	401.74	<0.001	1=3<2	381.23	391.79	362.14	0.103	-
Fusiform	2876.81	3032.31	2870.10	<0.001	1<3<2	2853.74	2941.51	2796.88	0.045	-
Inferior parietal	4098.60	4345.98	4231.19	<0.001	1<2=3	4797.20	5195.31	4862.88	<0.001	1<3<2
Inferior temporal	3113.24	3348.28	3184.90	<0.001	1<2=3	2971.57	3184.88	3044.48	<0.001	1<2=3
Isthmus cingulate	967.93	1033.00	971.29	<0.001	1<2=3	890.35	942.85	891.56	0.002	-
Lateral occipital	4590.66	4883.20	4692.66	<0.001	1<2=3	4616.80	4786.56	4607.65	0.053	-
Lateral orbitofrontal	2376.78	2577.58	2461.61	<0.001	1<2=3	2315.06	2549.14	2416.90	<0.001	1<3<2
Lingual	2830.63	3026.23	2859.44	<0.001	1=3<2	2952.02	3167.60	3013.88	0.001	1<2=3
Medial orbitofrontal	1854.35	1904.28	1857.69	0.018	-	1912.85	1999.00	1924.56	<0.001	1<3<2
Middle temporal	2867.12	3039.65	2972.65	<0.001	1<2=3	3119.69	3348.03	3225.53	<0.001	1<2=3
Parahippocampal	613.21	648.30	618.94	0.001	1=3<2	595.81	618.15	609.94	0.02	-
Paracentral	1225.98	1255.05	1245.10	0.196	-	1308.95	1362.49	1341.26	0.04	-
Pars opercularis	1401.65	1488.40	1449.48	0.012	-	1222.05	1269.52	1262.10	0.028	-
Pars orbitalis	601.69	639.08	609.07	<0.001	1<2=3	711.41	762.37	720.30	<0.001	1<3<2
Pars triangularis	1174.83	1259.99	1197.48	0.001	1<2=3	1429.27	1487.22	1440.67	0.166	-
Pericalcarine	1355.95	1443.16	1369.38	0.047	-	1511.52	1621.70	1527.90	0.004	-
Postcentral	3830.70	3999.30	3899.47	0.004	-	3729.31	3874.00	3793.81	0.03	-
Posterior cingulate	1060.48	1131.97	1080.63	0.007	-	1078.41	1164.84	1117.26	0.001	1<2=3
Precentral	4467.59	4678.91	4578.92	<0.001	1<2=3	4389.45	4616.70	4507.60	<0.001	1<2=3
Precuneus	3510.66	3739.06	3508.24	<0.001	1<2=3	3651.23	3865.98	3685.08	<0.001	1<2=3
Rostral anterior cingulate	745.15	815.70	760.69	0.002	-	557.38	613.97	577.36	0.002	-
Rostral middle frontal	4897.29	5286.43	5073.70	<0.001	1<2=3	4927.78	5169.80	5055.21	0.023	-
Superior frontal	6327.30	6660.35	6498.40	<0.001	1<2=3	6044.13	6162.24	6086.99	0.058	-
Superior parietal	4956.66	5238.93	5020.42	0.003	-	4777.99	5053.44	4875.15	0.004	-
Superior temporal	3622.98	3777.34	3709.77	<0.001	1<2=3	3376.80	3540.07	3467.85	<0.001	1<2=3
Supramarginal	3704.23	3938.31	3818.68	0.005	-	3275.37	3488.20	3417.71	<0.001	1<2=3
Frontal pole	253.08	256.38	255.97	0.087	-	316.33	321.23	312.53	0.381	-
Temporal pole	506.94	533.50	509.17	0.008	-	508.45	511.84	502.14	0.612	-
Transverse temporal	429.15	444.02	440.12	0.022	-	306.05	324.20	317.90	<0.001	1<2=3
Insula	2253.14	2365.17	2272.75	<0.001	1<2=3	2195.83	2269.87	2199.78	0.002	-

[&]p value was calculated with one-way ANOVA, and Bonferroni correction was applied to adjust for multiple comparisons of 34 regions on each hemisphere, a $p \leq 0.001$ is considered statistical significance.

[@]Bonferroni correction was applied to adjust for multiple comparisons of three groups, significance was thresholded at $p < 0.017$.

Table S5. Volume of cortical regions in Biotype1, Biotype 2 and control.

Label	Left hemisphere (mean, mm ³)					Right hemisphere (mean, mm ³)				
	Biotype1	Biotype2	Control	p value ^{&}	Post-hoc [@]	Biotype1	Biotype2	Control	p value ^{&}	Post-hoc [@]
Banks STS	1986.73	2072.01	2027.79	0.259	-	1792.35	1917.70	1861.65	0.022	-
Caudal anterior cingulate	1427.79	1448.16	1471.18	0.453	-	1759.62	1929.98	1799.21	0.009	-
Caudal middle frontal	5264.38	5533.88	5529.74	0.003	-	4884.99	5133.00	5194.21	<0.001	-
Cuneus	2723.38	2839.52	2716.13	0.166	-	3060.56	3176.23	3051.67	0.266	-
Entorhinal	1826.00	2024.17	1909.63	<0.001	1<2=3	1895.62	1930.41	1805.83	0.233	-
Fusiform	8762.29	9163.97	8720.21	0.013	-	8757.05	8965.13	8479.11	0.164	-
Inferior parietal	10385.94	11019.69	10876.10	0.001	1<2=3	12386.43	13469.41	12644.38	<0.001	1=3<2
Inferior temporal	10069.09	10717.84	10337.30	0.001	1<2=3	9673.28	10230.19	10031.11	0.001	1<2=3
Isthmus cingulate	2393.91	2524.66	2417.37	0.006	-	2203.90	2319.58	2235.11	0.008	-
Lateral occipital	10619.23	11085.40	10714.88	0.037	-	11024.98	11238.23	10974.85	0.448	-
Lateral orbitofrontal	6486.95	6878.52	6643.56	<0.001	1<2=3	6417.26	6906.35	6622.44	<0.001	1<2=3
Lingual	5611.17	5972.42	5634.41	0.01	-	6072.19	6383.17	6115.43	0.046	-
Medial orbitofrontal	4853.90	4915.67	4895.13	0.039	-	5174.86	5265.71	5192.26	0.062	-
Middle temporal	9554.16	10009.01	10009.18	<0.001	1<2=3	10329.06	11056.80	10779.44	<0.001	1<2=3
Parahippocampal	1745.81	1879.90	1781.15	0.004	-	1669.55	1770.48	1752.66	0.007	-
Paracentral	3278.36	3347.36	3282.74	0.766	-	3509.20	3660.30	3576.09	0.201	-
Pars opercularis	3942.00	4110.38	4053.45	0.094	-	3401.93	3513.36	3494.25	0.14	-
Pars orbitalis	2001.37	2086.06	1998.54	0.071	-	2377.09	2479.02	2390.64	0.066	-
Pars triangularis	3099.15	3297.55	3169.33	0.009	-	3904.60	3969.70	3882.29	0.765	-
Pericalcarine	1835.48	1886.55	1787.12	0.486	-	2157.26	2241.17	2121.86	0.282	-
Postcentral	8699.95	9033.50	8862.01	0.11	-	8399.40	8746.30	8540.02	0.095	-
Posterior cingulate	2712.92	2844.12	2753.37	0.113	-	2755.38	2972.34	2871.10	0.004	-
Precentral	12296.17	12940.34	12661.40	0.004	-	11689.42	12531.71	11997.38	0.001	1<2, 1=3, 2=3
Precuneus	8366.12	8938.00	8495.85	<0.001	1<2=3	8724.03	9297.37	8909.61	<0.001	1<2=3
Rostral anterior cingulate	2224.13	2417.66	2288.66	0.004	-	1757.93	1928.44	1799.18	0.005	-
Rostral middle frontal	13260.86	13833.02	13442.24	0.031	-	13879.69	14071.92	13874.70	0.326	-
Superior frontal	19962.72	20485.09	20175.75	0.033	-	18980.40	19006.71	18921.56	0.26	-
Superior parietal	11551.72	12125.55	11767.71	0.053	-	10811.40	11616.98	11246.59	0.003	-
Superior temporal	10738.07	11179.49	11080.79	0.008	-	10180.07	10698.30	10522.06	<0.001	1<2=3
Supramarginal	9838.98	10466.24	10212.37	0.01	-	8579.42	9195.12	9022.43	<0.001	1<2=3
Frontal pole	945.65	905.81	921.67	0.215	-	1186.52	1140.31	1153.13	0.382	-
Temporal pole	2601.36	2706.47	2669.75	0.129	-	2614.50	2727.85	2677.60	0.064	-
Transverse temporal	1046.10	1066.41	1046.65	0.759	-	767.13	797.64	786.07	0.2	-
Insula	6456.78	6725.28	6511.17	<0.001	1<2=3	6345.74	6531.91	6408.29	0.003	-

[&]p value was calculated with one-way ANOVA, and Bonferroni correction was applied to adjust for multiple comparisons of 34 regions on each hemisphere, a $p \leq 0.001$ is considered statistical significance.

[@]Bonferroni correction was applied to adjust for multiple comparisons of three groups, significance was thresholded at $p < 0.017$.

Table S6. Subcortical volume (mean, mm³) in Biotype 1, Biotype 2 and control.

	Biotype 1	Biotype 2	Control	<i>p</i> value	Post-hoc [@]
L-Cerebellum	49558.52	52350.40	51185.33	<0.001 ^{&}	1<2=3
L-Thalamus	6804.39	7350.91	7188.58	<0.001 ^{&}	1<2=3
L-Caudate	3007.83	3244.87	3187.05	<0.001 ^{&}	1<2=3
L-Putamen	4170.92	4566.53	4448.42	<0.001 ^{&}	1<2=3
L-Pallidum	1910.28	2022.44	1958.67	0.001 ^{&}	1<2=3
Brainstem	20208.94	21332.11	20884.29	<0.001 ^{&}	1<2=3
L-Hippocampus	3691.23	3999.65	3951.14	<0.001 ^{&}	1<2=3
L-Amygdala	1415.79	1537.26	1523.78	<0.001 ^{&}	1<2=3
L-Accumbens	287.13	334.53	334.40	<0.001 ^{&}	1<2=3
L-Ventral DC	3829.08	4033.39	3949.12	<0.001 ^{&}	1<2=3
R-Cerebellum	50811.37	52876.30	51877.91	0.007 ^{&}	-
R-Thalamus	6878.99	7459.46	7218.10	<0.001 ^{&}	1<2=3
R-Caudate	3033.63	3257.44	3183.87	0.001 ^{&}	1<2=3
R-Putamen	4256.54	4607.26	4493.26	<0.001 ^{&}	1<2=3
R-Pallidum	1882.49	1961.79	1929.42	0.023 ^{&}	-
R-Hippocampus	3869.60	4178.17	4128.86	<0.001 ^{&}	1<2=3
R-Amygdala	1633.25	1721.84	1710.33	<0.001 ^{&}	1<2=3
R-Accumbens	397.59	449.82	445.73	<0.001 ^{&}	1<2=3
R-Ventral DC	3735.59	3990.02	3901.87	<0.001 ^{&}	1<2=3
CC_Posterior	972.13	1021.63	1019.60	0.022 [%]	-
CC_Mid_Posterior	501.39	540.11	516.49	0.134 [%]	-
CC_Central	504.99	579.43	567.65	0.003 [%]	1<2=3
CC_Mid_Anterior	469.43	565.43	546.49	<0.001 [%]	1<2=3
CC_Anterior	812.10	851.36	856.28	0.013 [%]	-

[&] *p* value was calculated with one-way ANOVA, and Bonferroni correction was applied to adjust for multiple comparisons of 10 regions on each hemisphere, a $p < 0.005$ is considered statistical significance.

[%] *p* value was calculated with one-way ANOVA, and Bonferroni correction was applied to adjust for multiple comparisons of 5 regions, a $p < 0.01$ is considered statistical significance.

[@] Bonferroni correction was applied to adjust for multiple comparisons of three groups, significance was thresholded at $p < 0.017$.

Abbreviations: L, left; R, right; CC, cingulate cortex.

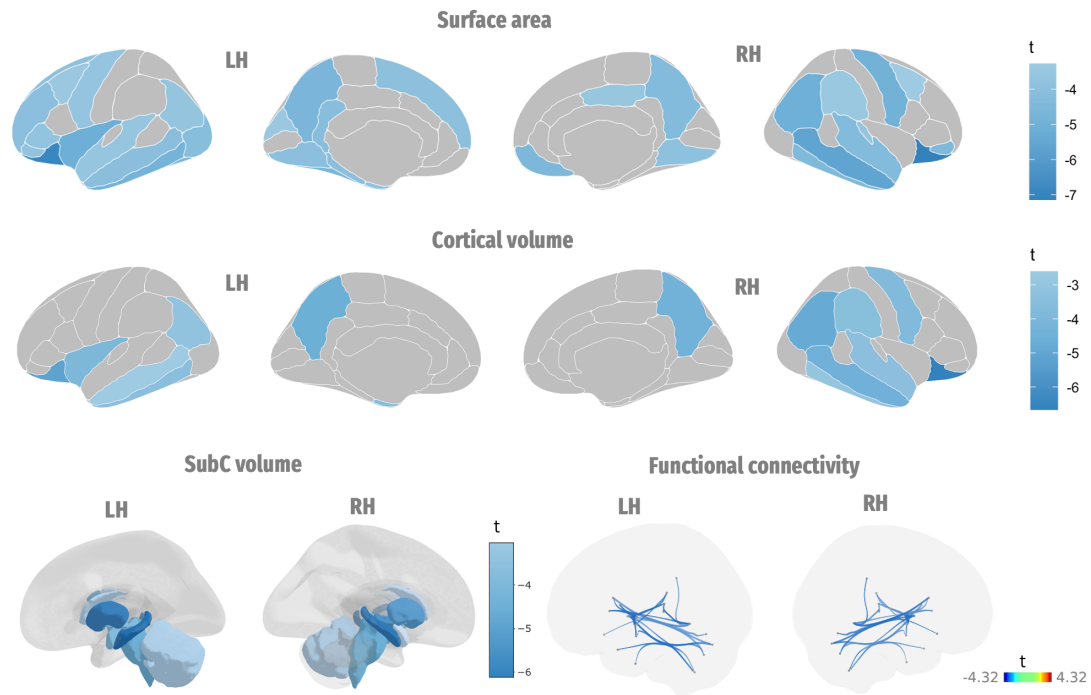


Fig. S1. Group differences of cortical surface area, volume, subcortical volume, and functional connectivity between Biotype 1 and Biotype 2 patients. The color bar represents t-statistics, with red indicating increase and blue indicating decrease. L/RH, left/right hemisphere.

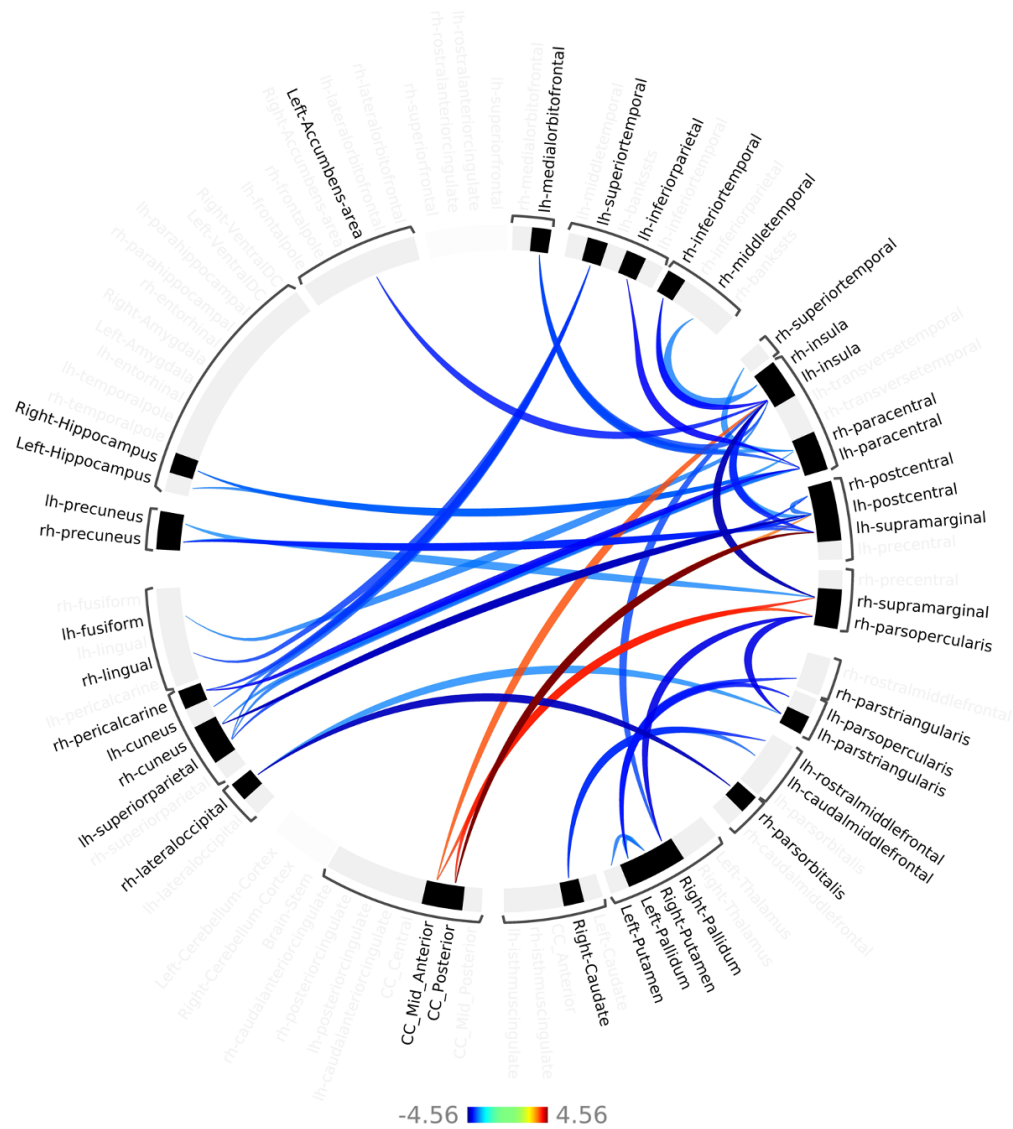


Fig. S2. Functional connectivity differences between Biotype 1 and the control group using Desikan-Killiany and aseg atlas. Only significant connections are displayed (thresholded at connection level $p < 0.001$ and multiple-comparison corrected using $p\text{-FDR} < 0.05$). The color bar represents t-statistics, with warm colors indicating hyperconnectivity and cold colors indicating hypoconnectivity.