**SUPPLEMENTARY METHODS**

**Image acquisition parameters and image quality inspection**

For the primary analyses of cross-sectional, longitudinal and lateralization comparisons, T1 weighted MPRAGE scans from the main cohort were collected using a 3-T Philips Achieva scanner (180 axial slices of 0.9 mm thickness with no gap, FOV = 230x230 mm2; TR=7.2 s, TI=856 ms, TE=3.8 ms, FA=8°, voxel size =0.9x0.9x0.9 mm3).

For the secondary linear discrimination analysis, T1 weighted MPRAGE scans from a smaller independent cohort were collected using Siemens Magnetom Prisma scanner (192 sagittal slices of 1.00 mm thickness FOV=256x256 mm2, TR=2300 ms, TI=900 ms, TE = 2.28ms, FA = 7°, voxel size = 1.0x1.0x1.0 mm3).

A three-step image quality control process was applied for images acquired from the initial 367 in both the primary and secondary cohorts (228 patients and 139 healthy controls). First, at both sites, images were inspected for motion artifact at the time of acquisition and scanning was repeated if necessary. Second, independent researchers visually inspected the raw DICOM structural images of individuals scanned before preprocessing. Of the original data from 318 collected using the Philips scanner, 2 were excluded after failing visual inspection for motion artifacts (ringing and ghosting); another 1 subject was excluded due to abnormally enlarged and anomalous shaped ventricles. These 3 excluded were patients with schizophrenia. Hence data from 187 patients (126 with schizophrenia/schizoaffective disorder, 46 with psychotic bipolar, 15 with brief psychotic disorder) and 125 healthy controls from the primary cohort were used for subsequent analysis. All the structural scans of the 52 of the secondary cohort (38 schizophrenia/schizoaffective disorder and 14 healthy controls) collected using the Siemens Prisma scanner passed visual quality checks.

After preprocessing, the images were subjected to another round of quality check using guidelines by the Enhancing NeuroImaging Genetics through Meta-Analysis (ENIGMA) Consortium (<http://enigma.ini.usc.edu>) (1). Subcortical data from the 312 passed the quality control guidelines. Not all cortical structure data passed the quality control process and were excluded; final sample size of each analysis was indicated by the statistical value of degrees of freedom in the corresponding tables.

**Table S1. A subset of 101 individuals with longitudinal data (at baseline)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Healthy** | **Preserved** | **Deteriorated** | **Compromised** | **χ2 or F value (d.f.)** | ***p* value** |
| **Demographics** |   |   |   |   |   |  |
| N | 44 | 26 | 20 | 11 | - |   |
| Gender | 24 m, 20 f | 12 m, 14 f | 7 m, 13 f | 6 m, 5 f | 2.32 (3) | .51 |
| Age (years) | 32.86 (9.94) | 32.52 (7.87) | 32.84 (8.75) | 43.03 (10.69) | 3.99 (3, 97) | .01a |
| Education (years) | 14.23 (2.27) | 12.54 (2.04) | 11.55 (1.70) | 10.91 (1.92) | 12.45 (3, 97) | <.001b |
| Ethnicity (C, M, I, O) | 39 C, 2 M, 2 I, 1 O | 26 C | 18 C, 1 M, 1 O | 11 C | 6.31 (9) | .71 |
| Handedness (R, L) | 40 R, 4 L | 22 R, 4 L | 20 R | 10 R, 1 L | 3.30 (3) | .35 |
| **Cognitive Measures** |   |   |   |   |   |   |
| WRAT3 | - | 50.69 (4.64) | 48.65 (5.20) | 40.27 (5.18) | 17.46 (2, 54) | <.001c |
| BAC verbal memory | - | -0.20 (0.97) | -1.69 (1.12) | -1.14 (0.77) | 13.12 (2, 54) | <.001d |
| BAC digit sequencing | - | 0.09 (1.00) | -.175 (1.00) | -1.37 (1.53) | 16.89 (2, 54) | <.001e |
| BAC token motor task | - | -0.81 (0.86) | -1.50 (1.2) | -1.2 (1.47) | 2.19 (2, 54) | .12 |
| BAC verbal fluency | - | -.042 (0.88) | -1.52 (0.98) | -1.21 (0.62) | 9.57 (2, 54) | <.001d |
| BAC symbol coding | - | -0.8 (1.00) | -1.98 (1.32) | -1.73 (0.81) | 7.27 (2, 54) | <.01f |
| BAC tower of london | - | 0.19 (1.03) | -2.29 (2.56) | -1.05 (0.81) | 12.05 (2,54) | <.001g |
| BAC composite | - | -0.32 (0.48) | -1.79 (0.94) | -1.28 (0.46) | 27.56 (2, 54) | <.001h |
| **Clinical measures** |   |   |   |   |   |   |
| Primary diagnosis (SZ, BD) | - | 18 SZ, 8 BD | 13 SZ, 7 BD | 6 SZ, 5 BD | 0.73 (2) | .69 |
| Age onset of illness | - | 25.63 (6.58) | 24.80 (5.67) | 29.09 (9.85) | 1.40 (2, 54) | .26 |
| Antipsychotic dosage (daily CPZ equivalent) | - | 293.27 (374.66) | 194.08 (205.46) | 94.09 (88.79) | 2.01 (2, 54) | .14 |
| Duration of illness in years | - | 5.85 (6.10) | 6.67 (5.81) | 12.49 (10.38) | 3.65 (2, 54) | .03i |
| PANSSPositive | - | 8.88 (2.96) | 9.20 (3.11) | 10.55 (4.25) | 1.01 (2, 54) | .37 |
| PANSS Negative | - | 8.08 (2.54) | 9.25 (4.63) | 8.00 (2.41) | 0.80 (2, 54) | .45 |
| PANSS General psychopathology | - | 19.88 (4.97) | 20.25 (3.67) | 19.18 (3.34) | 0.22 (2, 54) | .80 |
| **Neuroimaging measures****(mm3)** |  |   |   |   |   |   |
| ICV | 1298879 (172116.7) | 1242631 (201628.4) | 1236168 (179199) | 1310768 (183992.5) | 0.96 (3, 97) | .41 |
| TBV  | 1082546 (109289.4) | 1044011 (108706) | 1015723 (88974.14) | 1081881 (114495.6) | 3.40 (3, 95) | .02j |
| **§**6.81 (3, 94) | <.001k |
| Total GM | 596337.5 (59882.59) | 573590.1 (55696.19) | 556338.9 (49499.64) | 588454.4 (60112.2) | 4.60 (3, 95) | <.01 |
| **§**7.15 (3, 94) | <.001l |
| Subcortical GM | 61039.77 (6077.05) | 60737.85 (5292.11) | 57186.65 (4596.29) | 60063.18 (5546.69) | 4.39 (3, 95) | <.01 |
| **§**5.23 (3, 94) | <.01k |
| Cortical WM | 438252.9 (53966.67) | 420051.4 (51173.46) | 408233.2 (44633.28) | 440683.1 (56829.52) | 2.54 (3, 95) | .06 |
| **§**4.36 (3, 94) | <.01 |

**Measures of continuous variables are indicated by mean ± standard deviation. Post-hoc tests indicate**

aC older than P and D (*p*<.05).

bH had higher years of education than the other groups (*p*<.01).

cC performed worse than other groups on WRAT3 (*p*<.001).

dP performed better than other groups (*p*<.05)

eP performed better than other groups (*p*<.01)

fP performed better than D (*p*<.01).

gP performed better than D (*p*<.001).

hP performed better than other groups (*p*<.001)

iC had longer duration of illnesses than P(*p*<.05).

**After adjusting for effects of age and sex, post-hoc Tukey’s tests indicate**

jC had higher TBV than D (*p*<.05).

**§When ICV was adjusted for besides age and sex, post-hoc Tukey’s tests indicate**

kD had lower TBV and Subcortical GM than P (*p*<.05).

lD had lower Total GM than H and C (*p*<.05).

**Abbreviations:** bipolar disorder with history of psychosis, BD; brief assessment of cognition, BAC; brief psychotic disorder, BPD; Chinese, C; chlorpromazine equivalent daily doses, CPZ; females, f; gray matter, GM; healthy control, H; Indian, I; intracranial volume, ICV; Left, L; Malay, M; Males, m; other ethnicities, O; Positive and Negative Syndrome Scale, PANSS; Right, R; schizophrenia, SZ; total brain volume, TBV; white matter, WM; wide Range Achievement Test 3 (Reading subtest), WRAT3

**Table S2. Characteristics of an independent cohort of 52 individuals with neuroimaging data collected on a different MRI scanner for exploratory analysis**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Healthy | Preserved | Deteriorated | Compromised | χ2 or F value (d.f.) | *p* value |
| **Demographics** |   |   |   |   |   |  |
| N | 14 | 10 | 16 | 12 | - |   |
| Gender | 8 m, 6 f | 4 m, 6 f | 10 m, 6 f | 8 m, 4 f | 1.83 (3) | .61 |
| Age (years) | 33.21 (4.82) | 35.06 (5.07) | 31.10 (6.67) | 41.00 (6.40) | 6.94 (3, 48) | .001a |
| Education (years) | 15.04 (3.48) | 13.8 (4.05) | 11.19 (3.63) | 11.13 (3.16) | 4.04 (3, 48) | .01b |
| Ethnicity | 13 C, 1 I | 8 C, 2 I | 12 C, 2 M, 2 I | 11 C, 1 I | 5.86 (6) | .44 |
| Handedness | 13 R, 1 L | 10 R | 14 R, 2 L | 11 R, 1 L | 1.37 (3) | .71 |
| **Cognitive Measures** |   |   |   |   |   |   |
| WRAT3 | 48.50 (5.97) | 46.60 (3.63) | 47.50 (4.18) | 38.67 (5.60) | 10.26 (3, 48) | <.001c |
| BAC verbal memory | 0.01 (0.78) | -0.01 (1.16) | -1.19 (0.84) | -1.71 (1.28) | 9.13 (3, 48) | <.001d,e,f |
| BAC digit sequencing | -0.25 (1.00) | -0.45 (1.15) | -1.53 (0.97) | -1.34 (1.21) | 4.78 (3, 48) | <.01d,e,f |
| BAC token motor task | 0.22 (1.07) | -.1.01 (1.06) | -2.10 (1.41) | -1.74 (1.20) | 10.30 (3, 48) | <.001d |
| BAC verbal fluency | -0.23 (1.28) | -0.92 (0.65) | -1.66 (0.75) | -1.83 (0.92) | 8.26 (3, 48) | <.001d |
| BAC symbol coding | 0.01 (1.26) | -1.15 (0.82) | -1.97 (0.71) | -1.82 (0.80) | 13.01 (3, 48) | <.001d |
| BAC tower of london | -0.32 (0.99) | -0.22 (0.91) | -2.03 (1.94) | -2.20(2.43) | 4.89 (3, 48) | <.01d,f |
| BAC composite | -0.08 (0.88) | -0.62 (0.31) | -1.75 (0.57) | -1.47 (1.33) | 16.67 (3, 48) | <.001d,e,f |
| **Clinical measures** |   |   |   |   |   |   |
| Age onset of illness | - | 24.10 (4.51) | 20.63 (4.57) | 28.45 (7.57) | 6.36 (2, 34) | .004h |
| Antipsychotic dosage (daily CPZ equivalent) | - | 637.50 (512.40) | 600.39 (384.77) | 678.18 (409.79) | 0.11 (2, 35) | .89 |
| Duration of illness in years | - | 10.96 (4.54) | 10.48 (5.26) | 11.91 (8.32) | 0.18 (2, 34) | .84 |
| PANSSPositive | - | 14.30 (5.56) | 17.50 (5.57) | 15.75 (5.43) | 1.07 (2, 35) | .35 |
| PANSS Negative | - | 15.40 (4.62) | 16.69 (4.99) | 15.50 (4.68) | 0.31 (2, 35) | .74 |
| PANSS General psychopathology | - | 31.70 (7.88) | 37.31 (9.09) | 31.58 (8.51) | 2.01 (2, 35) | .15 |
| **Neuroimaging measures****(mm3)** |   |   |   |   |   |   |
| ICV | 1454759.83 (123806.72) | 1345599.92 (247917.13) | 1325774.40 (219147.85) | 1334350.93 (118647.62) | 1.50 (3, 48) | .23 |
| TBV | 1163181.64 (98352.27) | 1082358.40 (130607.69) | 1087703.19 (117571.84) | 1077260.67 (53849.39) | 3.80 (3, 46) | <.05 |
| **§**7.28 (3, 45) | <.001i |
| Total GM | 637207.08 (50635.64) | 582733.36 (70060.61) | 579351.47 (68603.56) | 564433.84 (33115.48) | 8.10 (3, 46) | <.001j |
| **§**14.01 (3, 45) | <.001k |
| Subcortical GM | 637207.08 (50635.64) | 582733.36 (70060.61) | 579351.47 (68603.56) | 564433.84 (33115.48) | 1.40 (3, 46) | .25 |
| **§**1.69 (3, 45) | .018 |
| Cortical WM | 476687.57 (53068.67) | 446168.20 (57134.16) | 462614.56 (58865.97) | 457210.83 (35348.78) | 1.02 (3, 46) | 0.39 |
| **§**1.33 (3, 45) | 0.28 |

**Measures of continuous variables are indicated by mean ± standard deviation. Post-hoc tests indicate**

aC older than H and D (*p* <.01).

bH received more years of education compared with D and C (*p* <.05).

cC scored lower in WRAT3 than H, P and D (*p*<.001).

dH performed better than D and C (*p*<.05). No significant differences found between H and P (*p* >.05)

eP performed better than D (*p*<.05).

fP performed better than C (*p*<.05).

gPost-hoc tests revealed no significant group differences.

hD had a lower age of onset than c (*p*<.01)

**After adjusting for effects of age and sex, post-hoc Tukey’s tests indicate**

jD and C showed lower total GM than H (*p*<.01).

**§When ICV was adjusted for besides age and sex, post-hoc Tukey’s tests indicate**

iD and C had lower TBV than H (*p*<.05).

kD and C showed lower total GM than H (*p*<.01).

**Abbreviations:** brief assessment of cognition, BAC; Chinese, C; chlorpromazine equivalent daily doses, CPZ; females, f; gray matter, GM; healthy control, H; Indian, I; intracranial volume, ICV; Left, L; Malay, M; Males, m; other ethnicities, O; Positive and Negative Syndrome Scale, PANSS; Right, R; total brain volume, TBV; white matter, WM; Wide Range Achievement Test 3 (Reading subtest), WRAT3

**Table S3: Characteristics of a subset of 214 young adults i.e. under 45 years of age. Patients had a primary diagnosis of schizophrenia.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Healthy | Preserved | Deteriorated | Compromised | χ2 or F value (d.f.) | *p* value |
| **Demographics** |   |   |   |   |   |  |
| N | 105 | 49 | 45 | 15 | - |   |
| Gender  | 68 m, 37 f | 25 m, 24 f | 29 m, 16 f | 10 m, 5 f | 3.08 (3) | .38 |
| Age (years) | 29.13 (4.81) | 30.60 (6.42) | 29.07 (5.75) | 31.57 (5.95) | 1.58 (3, 210) | .19 |
| Education (years) | 15.16 (2.27) | 12.74 (2.38) | 11.2 (2.32) | 10.2 (3.14) | 42.46 (3, 210) | <.001a |
| Ethnicity | 92 C, 4 M, 7 I, 2 O | 44 C, 2 M, 2I, 1 O | 37 C, 5 M, 2 I, 1 O | 13 C, 2 M | 6.27 (9) | .71 |
| Handedness | 99 R, 6 L | 45 R, 4 L | 44 R, 1 L | 13 R, 1 L, 1 A | 14.97 (6) | .02 |
| **Cognitive Measures** |   |   |   |   |   |   |
| WRAT3 | - | 50.71 (4.62) | 49.42 (4.59) | 35.20 (5.65) | 64.32 (2, 106) | <.001b |
| BAC verbal memory | - | -0.26 (0.89) | -1.56 (0.94) | -1.67 (1.08) | 27.23 (2, 106) | <.001c |
| BAC digit sequencing | - | 0.13 (0.93) | -1.50 (0.98) | -1.72 (1.28) | 38.46 (2, 106) | <.001c |
| BAC token motor task | - | -0.78 (0.95) | -1.24 (1.00) | -1.58 (1.19) | 4.61 (2, 106) | .012d |
| BAC verbal fluency | - | -0.36 (0.91) | -1.47 (1.02) | -1.71 (0.96) | 20.32 (2, 106) | <.001c |
| BAC symbol coding | - | -0.82 (0.87) | -2.01 (0.86) | -1.66 (0.90) | 22.47 (2, 106) | <.001c |
| BAC tower of london | - | 0.30 (0.93) | -1.64 (2.06) | -1.12 (2.39) | 15.81 (2, 106) | <.001c |
| BAC composite | - | -0.30 (0.39) | -1.57 (0.57) | -1.58 (0.69) | 82.04 (2, 106) | <.001c |
| **Clinical measures** |   |   |   |   |   |   |
| Age onset of illness | - | 24.51 (6.57) | 23.69 (4.98) | 26.80 (5.14) | 1.64 (2, 106) | .20 |
| Antipsychotic dosage (daily CPZ equivalent) | - | 314.37 (411.30) | 197.22 (182.88) | 230.17 (177.38) | 1.755 (2, 106) | .18 |
| Duration of illness in years | - | 5.34 (4.07) | 4.98 (4.73) | 4.30 (5.83) | 0.298 (2, 106) | .74 |
| PANSSPositive | - | 9.92 (3.30) | 10.62 (3.41) | 11.53 (4.73) | 1.29 (2, 106) | .28 |
| PANSS Negative | - | 9.12 (3.64) | 9.20 (2.83) | 9.87 (3.46) | 0.30 (2, 106) | .74 |
| PANSS General psychopathology | - | 20.43 (4.20) | 21.44 (3.41) | 21.80 (5.52) | 1.03 (2, 106) | .36 |
| **Neuroimaging measures****(mm3)** |  |   |   |   |   |   |
| ICV | 1285703 (173827.9) | 1232740 (186571.1) | 1300737 (196044.9) | 1189182 (193481.1) | 2.33 (3, 210) | .075 |
| TBV  | 1098250 (99762.02) | 1039204 (93733.99) | 1061785 (105780.6) | 1013024 (110536.1) | 8.95 (3, 208)23.22 (3, 207) | <.001e |
| <.001f |
| Total GM | 600971.9 (52825.88) | 561700.8 (48580.54) | 572663.1 (59014.87) | 553658.7 (56826.72) | 13.38 (3, 208)**§**27.51 (3, 207) | <.001g |
| <.001h |
| Subcortical GM | 61646.67 (4934.37) | 59511.41 (5235.53) | 60260.44 (5301.42) | 57073.67 (5135.94) | 6.49 (3, 208)**§**10.68 (3, 207) | <.001i |
| <.001j |
| Cortical WM | 450707.3 (49818.24) | 428281.4 (45789.68) | 438845.5 (48985.42) | 419079.5 (58933.12) | 4.62 (3, 208)**§**8,51 (3, 207) | <.01k |
| <.001l |

**Measures of continuous variables are indicated by mean ± standard deviation. Post-hoc tests indicate**

aH received more years of education compared with all the patient subtypes (*p*<.001), and P received more years of education compared with D (*p*<.05) and C (*p*<.005).

bC scored lower in WRAT than P and D (*p<.001*).

cP performed better than D and C (*p* <.001)

dP performed better than C (*p*=.022).

**After adjusting for effects of age and sex, post-hoc Tukey’s tests indicate:**

eC and P had lower TBV than H (*p*<.05).

gH had higher total GM than all patient subtypes (*p*<.01).

iC showed lower subcortical GM than H (*p*<.01)

kC showed lower cortical WM than H (*p*<.05).

**§When ICV was adjusted for besides age and sex, post-hoc Tukey’s tests indicate:**

fP and D had lower TBV than (*p*<.01).

hP and D showed lower total GM than H (*p*<.001).

jD showed lower subcortical GM than H (*p*<.05).

lD showed lower cortical WM than H (*p*<.05).

**Abbreviations:** ambidextrous, A; brief assessment of cognition, BAC; Chinese, C; chlorpromazine equivalent daily doses, CPZ; females, f; gray matter, GM; healthy control , H; Indian, I; intracranial volume, ICV; Left, L; Malay, M; Males, m; other ethnicities, O; Positive and Negative Syndrome Scale, PANSS; Right, R; total brain volume, TBV; white matter, WM; Wide Range Achievement Test 3 (Reading subtest), WRAT3

**Table S4. Summary statistics of different cognitive groups in the subset of 212 young adults with schizophrenia and healthy comparison controls.**

|  |  |  |
| --- | --- | --- |
|   | **aF and p-values of ANOVA test of cognitive subtype; Cohen’s f2** | **bPost-hoc pairwise tests (multiple comparisons corrected)** |
|  |  | P vs H | D vs H | C vs H | D vs P | C vs P | C vs D |
| **Hippocampus** |  |  |  |  |  |  |  |
| left | F3, 205=20.89, ***p*=7.6e-12#**; ƒ2=0.15 | β=-174.73, SE=60.03, *t*=-2.91, ***p*=.020\*** | β=-346.28, SE=61.99, *t*=-5.59, ***p*<.001\*\*\***  | β=-247.74, SE=91.41, *t*=-2.71, ***p*=.035\***  | β=-171.55, SE=60.09, *t*=-2.85, ***p*=.023\***  | β=-73.01, SE=85.68, *t*=-0.85, *p*=.83 | β=98.54, SE=85.61, *t*=1.15, *p*=.65 |
| right | F3, 205=15.37, ***p*=4.7e-09#**; ƒ2=0.12 | β=-131.10, SE=66.04, *t*=-1.99, *p*=.19 | β=-268.28, SE=68.20, *t*=-3.93, ***p*<.001\*\*\*** | β=-308.14, SE=100.56, *t*=-3.06, ***p*=.013\***  | β=-137.19, SE=66.10, *t*=-2.08, *p*=.16 | β=-177.04, SE=94.25, *t*=-1.88, *p*=.24 | β=-39.86, SE=94.17, *t*=-0.42, *p*=.98 |
| Amygdala |  |  |  |  |  |  |  |
| left | F3, 205=6.60, ***p*=.000028#**; ƒ2=0.07 | β=6.71, SE=42.80, *t*=0.091, *p*=1.00 | β=-69.44, SE=44.20, *t*=-1.57, *p=*.39 | β=-118.78, SE=65.18, *t*=-1.82, *p*=.26 | β=-76.16, SE=42.84, *t*=-1.78, *p*=.28 | β=-125.49, SE=61.09, *t*=-2.05, *p*=.17  | β=-49.33, SE=61.04, *t*=-0.81, *p*=.85 |
| right | F3, 205=3.66, *p*=.04 | β=-45.06, SE=48.12, *t*=-0.94, *p*=.78 | β=-57.06, SE=49.69, *t*=-1.15, *p=*.65 | β=-29.81, SE=73.27, *t*=-0.41, *p*=.98 | β=-12.00, SE=48.17, *t*=-0.25, *p*=.99 | β=15.24, SE=68.67, *t*=0.22, *p*=.99  | β=27.24, SE=68.62, *t*=0.40, *p*=.98 |
| **Thalamus** |  |  |  |  |  |  |  |
| left | F3, 205=9.29, ***p*=9.85e-05#**; ƒ2=0.09 | β=-393.02, SE=163.67, *t*=--2.40, *p*=.08 | β=-439.99, SE=169.01, *t*=-2.60, ***p=*.047\*** | β=-607.27, SE=249.21, *t*=-2.44, *p*=.07  | β=-46.97, SE=163.82, *t*=-0.29, *p*=.99 | β=-214.25, SE=233.58, *t*=-0.92, *p*=.79 | β=-167.28, SE=233.39, *t*=-0.72, *p*=.89 |
| right | F3, 205=22.62, ***p*=1.1e-12#**; ƒ2=0.17 | β=-325.52, SE=109.84, *t*=-2. 96, ***p*=.017\*** | β=-327.39, SE=113.42, *t*=-2.89, ***p=*.021\***  | β=-399.07, SE=167.24, *t*=-2.39, *p*=.08 | β=-1.87, SE=109.93, *t*=-0.02, *p*=1.0 | β=-73.55, SE= 156.75, *t*=-0.47, *p*=.96 | β=-71.69, SE=156.62, *t*=-0.46, *p*=.97 |
| **Lateral ventricles** |  |  |  |  |  |  |  |
| Left | F3, 205=6.57 , ***p*=.00029#**; ƒ2=0.06 | β=2994.2, SE=668.1, *t*=4.45, ***p*<0.001 \*\*\*** | β=2527.6, SE=689.9, *t*=3.67, ***p=.0017\**** | β=2748.0, SE=1017.3, *t*=2.69, ***p*=.*0.036\****  | β=-466.6, SE=668.7, *t*=-0.69, *p*=.90 | β=-246.2, SE=953.5, *t*=-0.28, *p*=.99  | β=220.4, SE=952.7, *t*=0.21, *p*=1.0 |
| Right | F3, 205=6.22, ***p*=.00046#**; ƒ2=0.07 | β=2250.6, SE=555.3, *t*=4.05, ***p*<0.001 \*\*\*** | β=2101.2, SE=573.4, *t*=3.67, ***p*=.0015\*\*** | β=1457.5, SE=845.5, *t*=1.72, *p*=.31 | β=-149.4, SE=555.8, *t*=-0.27, *p*=1.0 | β=-793.1, SE=792.4, *t*=-1.00, *p*=.74  | β=-643.7, SE= 791.8, *t*=-0.81, *p*=.84 |

|  |  |  |
| --- | --- | --- |
| **B) Thickness of cortical regions** | **1F and p-values of ANOVA test of cognitive subtype; Cohen’s** ƒ2 | **2Post-hoc pairwise tests**  |
|  |  | **P vs H** | **D vs H** | **C vs H** | **D vs P** | **C vs P** | **C vs D** |
| **Banks of the superior temporal sulcus** |  |  |  |  |  |  |  |
| left | F3, 165=8.95, ***p*=** **1.58e-05#**; ƒ2=0.13 | β=-0.10, SE=0.03, t=-3.34, **p=.0053\*\*** | β=-0.15, SE=0.03, t=-4.40, **p<.001\*\*\*** | β=-0.09, SE=0.05, t=-1.72, p=.31 | β=-0.05, SE=0.03, t=-1.54, p=.411 | β=0.006, SE=0.05, t=0.12, p=.99 | β=0.06, SE=0.05, t=2.22, p=0.67 |
| right | F3, 191=8.34, ***p*=** **3.076e-05#**; ƒ2=0.10 | β=-0.08, SE=0.03, t=-2.47, p=.06 | β=-0.13, SE=0.04, t=-3.71, **p=.0013\*\*** | β=-0.10, SE=0.05, t=-2.10, p=.16 | β=-0.05, SE=0.04, t=-1.60, p=.37 | β=0.02, SE=0.05, t=-0.58, p=0.93 | β=0.03, SE=0.05, t=0.58, p=.939 |
| **Caudal anterior cingulate gyrus** |  |  |  |  |  |  |  |
| left | F3, 207=1.99, *p*=.12  |  |  |  |  |  |  |
| right | F3, 207=3.24, *p*=.023 |  |  |  |  |  |  |
| **Caudal middle frontal gyrus** |  |  |  |  |  |  |  |
| left | F3, 207=4.03, *p*=.008  |  |  |  |  |  |  |
| right | F3, 207=4.67, *p*=.0035 |  |  |  |  |  |  |
| **Cuneus**  |  |  |  |  |  |  |  |
| Left | F3, 205=7.42, ***p*=9.70e-05#**; ƒ2=0.09 | β=-0.08, SE=0.02, t=-3.3, **p=.005\*** | β=-0.05, SE=0.03, t=-2.0, p=.17 | β=-0.08, SE=0.04, t=-2.0, p=.18 | β=0.02, SE=0.03, t=0.98, p=.76 | β=0.002, SE=0.04, t=0.07, p=.99 | β=-0.02, SE=0.05, t=-0.07, p=0.87 |
| Right | F3, 207=6.52, ***p*=.00031#**; ƒ2=0.09 | β=-0.07 SE=0.02, t=-3.01, **p=.01\*** | β=-0.09, SE=0.03, t=-3.39, **p=.005\*** | β=-0.07, SE=0.04, t=-1.92 p=.21 | β=-0.02, SE=0.03, t=-0.59, p=.93 | β=0.0, SE=0.04, -t=0.03, p=1.0 | β=0.01, SE=0.04, t=0.38, p=.984 |
| **Entorhinal cortex** |  |  |  |  |  |  |  |
| left | F3, 207=0.74, *p*=.53 |  |  |  |  |  |  |
| right | F3, 207=0.52, *p*=.67 |  |  |  |  |  |  |
| **Fusiform gyrus** |  |  |  |  |  |  |  |
| left | F3, 206=6.82, ***p*=.0002#,**ƒ2=0.08 |  |  |  |  |  |  |
| right | F3, 207=10.40, ***p*=2.10e-06**#, ƒ2=0.10 |  |  |  |  |  |  |
| **Inferior parietal cortex** |  |  |  |  |  |  |  |
| Left | F3, 206=7.72, ***p*=6.50e-05#;** ƒ2=0.10 | β=-0.10, SE=0.02, t=-3.96, **p<.001\*\*\*** | β=-0.93, SE=0.03, t=-3.41, **p=.004\*** | β=-0.04, SE=0.04, t=-1.07, p=.70 | β=-0.03, SE=0.03, t=-1.06, p=.99 | β=0.05, SE=0.04, t=0.13, p=.51 | β=0.05, SE=0.04, t=1.37, p=.56 |
| right | F3, 207=7.33, ***p=*.0001#,**ƒ2=0.08 | β=-0.06, SE=0.02, t=-2.91, **p=.02\*** | β=-0.08, SE=0.03, t=-3.01, **p=.01\*** | β=-0.04, SE=0.04, t=-0.96, p=.77 | β=-0.01, SE=0.4 t=-0.48, p=.96 | β=0.03, SE=0.04, t=0.83, p=.83 | β=0.04, SE=0.04, t=1.18, p=.63 |
| **Inferior temporal gyrus** |  |  |  |  |  |  |  |
| left | F3, 198=4.14, *p*=.0071 |  |  |  |  |  |  |
| right | F3, 199=4.31, *p*=.0057 |  |  |  |  |  |  |
| **Isthmus cingulate gyrus** |  |  |  |  |  |  |  |
| left | F3, 207=1.09, *p*=.36 |  |  |  |  |  |  |
| right | F3, 207=4.45, *p*=.0046 |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| **Lateral occipital gyrus** |  |  |  |  |  |  |  |
| Left | F3, 207=9.75, ***p*=** **4.78e-06#**; ƒ2=0.11 | β=-0.11, SE=0.02, t=-4.56, **p<.001\*\*\*** | β=-0.10, SE=0.02, t=-3.8, **p<.001\*\*\*** | β=-0.06, SE=0.03, t=-1.58, p=.38 | β=-0.007, SE=0.02, t=-0.26, p=.99 | β=0.05, SE=0.04, t=1.21, p=.61 | β=0.03, SE=0.04, t=1.046, p=.71 |
| Right | F3, 207=7.68, ***p*=6.89e-05#**; ƒ2=0.09 | β=-0.10, SE=0.02, t=-3.86, **p=.001\*\*** | β=-0.10, SE=0.03, t=-3.56, **p=.0023\*\*** | β=-0.06, SE=0.04, t=-1.47, p=.45 | β=-0.002, SE=0.03, t=-0.10, p=1.0 | β=0.04, SE=0.04, t=0.89, p=.80 | β=0.04, SE=0.04, t=0.97, p=.76 |
| **Lateral orbitofrontal gyrus** |  |  |  |  |  |  |  |
| Left | F3, 207=9.48, ***p*=6.75e-06****#**; ƒ2=0.10 | β=-0.09, SE=0.03, t=-3.45, **p=.0037\*\*** | β=-0.10, SE=0.03, t=-3.48, **p=.0032\*\*** | β=-0.11, SE=0.04, t=-2.67, **p=.039\*\*** | β=-0.01, SE=0.03, t=-0.39, p=0.97 | β=-0.02, SE=0.04, t=-0.61, p=.93 | β=-0.01, SE=0.04, t=-0.34, p=.99 |
| Right | F3, 206=9.40, ***p*=7.48e-06****#**; ƒ2=0.10 | β=-0.06, SE=0.02, t=-2.21, p=.12 | β=-0.10, SE=0.03, t=-3.84, **p<0.001\*\*\*** | β=-0.09, SE=0.04, t=-2.14, p=.14 | β=-0.05, SE=0.03, t=-1.91, p=.22 | β=-0.03, SE=0.04, t=-0.85, p=0.83 | β=0, SE=0.04, t=0.48, p=0.96 |
| **Lingual gyrus** |  |  |  |  |  |  |  |
| Left | F3, 207=8.72, ***p*=1.78e-05#**; ƒ2=0.10 | β=-0.06, SE=0.02, t=-2.77, **p=0.03\*** | β=-0.07, SE=0.02, t=-2.77, **p=.03\*** | β=-0.13, SE=0.04, t=-3.36, **p=.004\*\*** | β=-0.007, SE=0.03, t=-0.29, p=0.99 | β=-0.06, SE=0.04, t=-1.75, p=0.29 | β=-0.06, SE=0.04, t=-1.57, p=.39 |
| Right | F3, 206=7.088, ***p*=****.** **00015#;** ƒ2=0.08 | β=-0.07, SE=0.02, t=-2.97, **p=0.02\*** | β=-0.06, SE=0.03, t=-2.29, p=.09 | β=-0.05, SE=0.04, t=-1.32, p=.54 | β=-0.01, SE=0.03, t=-0.38, p=0.98 | β=0.02, SE=0.04, t=0.49, p=0.96 | β=0.08, SE=0.04, t=0.23, p=1.0 |
| **Medial orbital frontal gyrus** |  |  |  |  |  |  |  |
| Left | F3, 206=10.08, ***p*=** **3.16e-06#**; ƒ2=0.11 | β=-0.06, SE=0.02, t=-2.5, p=0.6 | β=-0.09, SE=0.03, t=-3.4, **p=.005\*\*** | β=-0.01, SE=0.04, t=-0.38, p=0.98 | β=0.03, SE=0.03, t=-1.13, p=0.66 | β=0.08, SE=0.04, t=1.96, p=.20 | β=0.11, SE=0.04, t=2.79, **p=.03\*** |
| Right | F3, 207= 6.52, ***p*=0.00031#**; ƒ2=0.08 | β=-0.06, SE=0.03, t=-2.09, p=.15 | β=-0.11, SE=0.03, t=-3.39, **p=.004\*\*** | β=-0.04, SE=0.05 t=-0.09, p=1.0 | β=-0.05, SE=0.03, t=-1.50, p=1.0 | β=0.06, SE=0.05, t=1.22, p=.43 | β=0.10, SE=0.05, t=2.30, p=.60 |
| **Middle temporal gyrus** |  |  |  |  |  |  |  |
| left | F3, 207=4.61, *p*=.004 |  |  |  |  |  |  |
| right | F3, 207=12.37, ***p*=1.79e-07#;** ƒ2=0.13 | β=-0.08, SE=0.03, t=-3.1, **p=.01\*** | β=-0.12, SE=0.03, t=-4.09, **p<0.001\*\*\*** | β=-0.08, SE=0.4 t=-1.75, p=.29 | β=-0.04, SE=0.03, t=-1.30, p=.55 | β=0.006, SE=0.04, t=0.14, p=.99 | β=0.05, SE=0.04, t=1.06, p=.70 |
| **Parahippocampal gyrus** |  |  |  |  |  |  |  |
| left | F3, 207=4.40, *p*=.005 |  |  |  |  |  |  |
| right | F3, 207=3.07, *p*=.029 |  |  |  |  |  |  |
| **Paracentral gyrus** |  |  |  |  |  |  |  |
| left | F3, 207=1.99, *p*=.11 |  |  |  |  |  |  |
| right | F3, 207=1.70, *p*=.17 |  |  |  |  |  |  |
| **Pars opercularis**  |  |  |  |  |  |  |  |
| Left | F3, 207=10.21, ***p*=2.67e-06#**; ƒ2=0.10 | β=-0.10, SE=0.02, t=-3.89,  **p<0.001\*\*\*** | β=-0.09, SE=0.03, t=-3.32, **p=.0055\*\*** | β=-0.08, SE=0.04, t=-2.04, p=.17 | β=0.004, SE=0.03, t=-0.17, p=1.0 | β=0.01, SE=0.04, t=0.32, p=.99 | β=0.008, SE=0.04, t=0.21, p=.99 |
| Right | F3, 207=7.77, ***p*=6.08e-05#**; ƒ2=0.10 | β=-0.10, SE=0.03, t=-3.60, **p=.002\*\*** | β=-0.13, SE=0.03, t=-4.15, **p<0.001\*\*\*** | β=-0.06, SE=0.05, t=-1.29, p=.56 | β=-0.03, SE=0.03, t=-0.94, p=.78 | β=0.04, SE=0.04, t=0.91, p=0.7 | β=0.07, SE=0.04, t=1.58, p=.38 |
| **Pars orbitalis** |  |  |  |  |  |  |  |
| Left | F3, 207=12.43, ***p*=**1.66e-07**#**; ƒ2=0.13 | β=-0.13, SE=0.04, t=-3.51, **p=.003\*\*** | β=-0.19, SE=0.04, t=-4.64, **p<0.001\*\*\*** | β=-0.17, SE=0.06, t=-2.74, **p=.03\*** | β=-0.06, SE=0.04, t=-1.51, p=.42 | β=0.04, SE=0.06, t=-0.65, p=0.91 | β=0.02, SE=0.06, t=0.40, p=.98 |
| Right | F3, 207=6.72, ***p*=.0002113#**; ƒ2=0.09 | β=-0.11, SE=0.04, t=-3.01, **p=.0014\*\*** | β=-0.17, SE=0.04, t=-4.19, **p<0.001\*\*\*** | β=-0.15, SE=0.06, t=-2.43, p=.07 | β=-0.06, SE=0.04, t=-1.49, p=.44 | β=-0.04, SE=0.06, t=-0.63, p=0.92 | β=0.02, SE=0.06, t=0.41, p=.98 |
| **Pars triangularis**  |  |  |  |  |  |  |  |
| Left | F3, 207=10.0, ***p*=3.97e-06#**; ƒ2=0.11 | β=-0.09, SE=0.03, t=-3.09, **p=.01\*** | β=-0.13, SE=0.03, t=-4.21, **p<0.001\*\*\*** | β=-0.098, SE=0.05, t=-2.11, p=0.15 | β=-0.05, SE=0.03, t=-1.46, p=.46 | β=-0.01, SE=0.04, t=-0.27, p=.99 | β=0.03, SE=0.04, t=0.76, p=.87 |
| Right | F3, 207=9.56, ***p*=****6.17e-06#**; ƒ2=0.11 | β=-0.07, SE=0.02, t=-2.87, **p=.02\*** | β=-0.13, SE=0.03, t=-4.85, **p<0.001\*\*\*** | β=-0.06, SE=0.04, t=-1.29, p=.56 | β=-0.05, SE=0.03, t=-1.85, p=.25 | β=0.02, SE=0.04, t=0.44, p=0.97 | β=0.07, SE=0.04, t=1.75, p=.29 |
| **Pericalcarine gyrus** |  |  |  |  |  |  |  |
| left | F3, 187=0.93, *p*=.43 |  |  |  |  |  |  |
| right | F3, 167=2.11, *p*=.10 |  |  |  |  |  |  |
| **Postcentral gyrus**  |  |  |  |  |  |  |  |
| left | F3, 207=1.51, *p*=.21 |  |  |  |  |  |  |
| right | F3, 206=2.89, *p*=.04 |  |  |  |  |  |  |
| **Posterior cingulate gyrus** |  |  |  |  |  |  |  |
| left | F3, 207=1.85, *p*=.14 |  |  |  |  |  |  |
| right | F3, 207=0.91, *p*=.43 |  |  |  |  |  |  |
| **Precentral gyrus** |  |  |  |  |  |  |  |
| left | F3, 207=5.97, ***p*=.00063#**; ƒ2=0.08 | β=-0.07, SE=0.03, t=-2.60, **p=.05\*** | β=-0.13, SE=0.03, t=-4.58, **p<0.001\*\*\*** | β=-0.08, SE=0.04, t=-1.69, p=0.32 | β=-0.07, SE=0.03, t=-2.26, p=.10 | β=-0.006, SE=0.04, t=-0.13, p=.99 | β=0.06, SE=0.04, t=1.46, p=.46 |
| right | F3, 207=7.12, ***p*=.0001#**; ƒ2=0.09 | β=-0.09, SE=0.03, t=-3.39, **p=.004\*\*** | β=-0.13, SE=0.03, t=-4.45, **p<0.001\*\*\*** | β=-0.10, SE=0.04, t=-2.39, p=.08 | β=-0.04, SE=0.03, t=-1.42, p=.48 | β=0.02, SE=0.04, t=-0.36, p=0.98 | β=0.03, SE=0.04, t=0.63, p=.92 |
| **Precuneus** |  |  |  |  |  |  |  |
| left | F3, 207=4.64, *p*=.0037 |  |  |  |  |  |  |
| right | F3, 207=4.85, *p*=.003 |  |  |  |  |  |  |
| **Rostral anterior cingulate gyrus** |  |  |  |  |  |  |  |
| left | F3, 207=0.60, *p*=.61 |  |  |  |  |  |  |
| right | F3, 207=3.60, *p*=.014  |  |  |  |  |  |  |
| **Rostral middle frontal gyrus** |  |  |  |  |  |  |  |
| Left | F3, 207=4.14, *p*=.007 |  |  |  |  |  |  |
| Right | F3, 207=9.07, ***p*=1.14e-05****#**; ƒ2=0.10 | β=-0.07, SE=0.02, t=-3.05, **p=.01\*** | β=-0.12, SE=0.03, t=-4.28, **p<0.001\*\*\*** | β=-0.05, SE=0.04, t=-1.30, p=.55 | β=-0.04, SE=0.03, t=-1.56, p=.40 | β=0.02, SE=0.04, t=0.56, p=.94 | β=0.06, SE=0.04, t=1.66, p=.34 |
| **Superior frontal  gyrus** |  |  |  |  |  |  |  |
| Left | F3, 207=6.50, ***p*=.00032#**; ƒ2=0.08 | β=-0.05, SE=0.03, t=-1.88, p=.27 | β=-0.10, SE=0.03, t=-3.10, **p=.0033\*\*** | β=-0.06, SE=0.05, t=-1.36, p=.35 | β=-0.04, SE=0.03, t=-1.43, p=.24 | β=-0.01, SE=0.04, t=-0.23, p=.99 | β=0.03, SE=0.04, t=0.77, p=.63 |
| Right | F3, 207=8.42, ***p*=2.62e-05#**; ƒ2=0.08 | β=-0.07, SE=0.03, t=-2.60, p=.047 | β=-0.13, SE=0.03, t=-4.57, **p<0.001\*\*\*** | β=-0.07, SE=0.05, t=-1.69, p=.32 | β=-0.07, SE=0.03, t=-2.26, p=.10 | β=-0.005, SE=0.04, t=-0.13, p=1.0 | β=0.06, SE=0.04, t=1.46, p=.46 |
| **Superior parietal gyrus** |  |  |  |  |  |  |  |
| left | F3, 207=5.51, *p*=.001 |  |  |  |  |  |  |
| right | F3, 207=2.91, *p*=.035 |  |  |  |  |  |  |
| **Superior temporal gyrus** |  |  |  |  |  |  |  |
| left | F3, 207=6.64, ***p*=.00027#;** ƒ2=0.08 | β=-0.09, SE=0.03, t=-3.39, **p=.004\*\*** | β=-0.13, SE=0.03, t=-4.452, **p<0.001\*\*\*** | β=-0.11, SE=0.04, t=-2.39, p=.08 | β=-0.04, SE=0.03, t=-1.42, p=.48 | β=0.02, SE=0.04, t=-0.36, p=.98 | β=0.03, SE=0.04, t=0.63, p=.92 |
| right | F3, 207=13.19, ***p*=6.50e-08#**; ƒ2=0.14 | β=-0.07, SE=0.02, t=-3.46, **p=.0033\*\*** | β=-0.11, SE=0.02, t=-4.62, **p<0.001\*\*\*** | β=-0.06, SE=0.03, t=-2.16, p=.13 | β=-0.04, SE=0.02, t=-1.56, p=.40 | β=0.01, SE=0.03, t=0.35, p=.98 | β=0.05, SE=0.03, t=1.62, p=.37 |
| **Supramarginal gyrus** |  |  |  |  |  |  |  |
| left | F3, 207=6.21, ***p*=.00046#**; ƒ2=0.08 |  |  |  |  |  |  |
| right | F3, 207=6.87, ***p*=.0002**#; ƒ2=0.09 |  |  |  |  |  |  |
| **Frontal pole**  |  |  |  |  |  |  |  |
| left | F3, 207=1.93, *p*=.12 |  |  |  |  |  |  |
| right | F3, 207=3.88, *p*=.01 |  |  |  |  |  |  |
| **Temporal pole**  |  |  |  |  |  |  |  |
| left | F3, 207=1.21 *p*=.31 |  |  |  |  |  |  |
| right | F3, 207=0.67, *p*=.57 |  |  |  |  |  |  |
| **Transverse temporal gyrus** |  |  |  |  |  |  |  |
| left | F3, 207=3.70, *p*=.01 |  |  |  |  |  |  |
| right | F3, 207=1.59, *p*=.19 |  |  |  |  |  |  |
| **Insula**  |  |  |  |  |  |  |  |
| left | F3, 201=3.77, *p*=.01 |  |  |  |  |  |  |
| right | F3, 201=2.93, *p*=.03 |  |  |  |  |  |  |

aTo determine the the effect of cognitive subtype to the brain volume variability, ANOVA F- values (between-group/within-group variances) **#** indicates a significant effect of cognitive subtype, Bonferroni-corrected for the multiple brain regions-of-interest. Cohen’s ƒ2 values (local effect size, i.e. effect size of an individual variable within a multivariate model) of cognitive subtypes are provided for the regions surviving multiple comparisons. ƒ2effect sizes of 0.02, 0.15, and 0.35 are termed *small*, *medium*, and *large*, respectively (3).

**b**Post-hoc analyses were conducted using Tukey’s and adjusted *p*-values of \*<.05, \*\*<.01 or \*\*\*<.001 shown.

Abbreviations: Beta coefficients, β; Compromised, C; Deteriorated, D; Healthy, H; Preserved, P; Standard Error, SE