**Figure S1. Vertex-wise whole-brain analysis for comparing the local gyrification index between patients with major depressive disorder and healthy control participants.** The vertex-wise whole brain analysis includes age, sex, and education years as covariates, and the results were corrected for multiple comparisons using a Monte Carlo simulation with 10,000 iterations, vertex-wise threshold of P < 0.001 and cluster-wise threshold of P < 0.05.

****

**Table S1. Vertex-wise comparison of local gyrification index between patients with major depressive disorder and healthy controls.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Cluster annotation** | **Max** | **Cluster Size (mm2)** | **MNI** | **Mainly involved structures** |
| **x** | **y** | **z** |
| ***Left hemisphere*** |  |  |  |  |  |  |
| Pars triangularis | -10.6352 | 5931 | -46.8 | 24.3 | 6.8 | Pars triangularis, Pars orbitalis, Pars opercularis, Middle Frontal  |
| Lingual gyrus | -7.1295 | 2890  | -16.5 | -79.3 | -11.7 | Lingual, Cuneus, Isthmus Cingulate |
| Inferior temporal gyrus | -3.5390 | 1056  | -55.4 | -43.9 | -13.9 |  |
| Precuneus | -3.1852 | 94  | -10.1 | -48.6 | 44.6 | Cuneus |
| Entorhinal cortex | -3.3133 | 93  | -28.7 | -8.3 | -32.9 |  |
| ***Right hemisphere*** |  |  |  |  |  |  |
| Lateral orbitofrontal cortex | -7.8770 | 3832  | 30.2 | 26.0 | -19.1 | Orbitofrontal, Insula, Pars triangularis  |
| Lingual gyrus | -4.6840 | 1803  | 10.2 | -70.9 | -3.1 |  |
| Inferior temporal gyrus | -3.2099 | 107 | 47.3 | -32.3 | -21.2 |  |
| Lateral occipital cortex | -3.2711 | 101 | 47.4 | -78.3 | 4.1 |  |

MNI coordinates refer to the vertex with the greatest difference in cortical metrics between the reading groups within a cluster.

Monte Carlo simulations were applied for cluster-wise correction.

**Table S2. Model 1: Comparison of local gyrification index between patients with major depressive disorders and healthy controls controlling for total intracranial cavity volume**

|  |  |  |  |
| --- | --- | --- | --- |
| **Cortical regions** | **MDD (n = 234)** | **HC (n = 215)** | **MDD vs. HC** |
| **mean** | **SD** | **mean** | **SD** | **F (1, 443)** | **P-value** | **Cohen's f** |
| ***Left hemisphere*** |  |  |  |  |  |  |  |
| L Caudal anterior cingulate cortex | 1.91 | 0.11 | 1.93 | 0.11 | 5.233  | 0.023  | 0.109 |
| **L Caudal middle frontal gyrus** | 3.19 | 0.21 | 3.27 | 0.19 | **22.075**  | **3.51.E-06** | 0.223 |
| L Cuneus | 3.06 | 0.20 | 3.10 | 0.19 | 3.536  | 0.061  | 0.089 |
| L Entorhinal cortex | 2.64 | 0.13 | 2.67 | 0.13 | 6.066  | 0.014  | 0.117 |
| L Fusiform gyrus | 2.78 | 0.12 | 2.81 | 0.11 | 11.160  | 0.001  | 0.159 |
| L Inferior parietal cortex | 3.36 | 0.19 | 3.41 | 0.17 | 10.185  | 0.002  | 0.152 |
| L Inferior temporal gyrus | 2.82 | 0.12 | 2.84 | 0.12 | 2.111  | 0.147  | 0.069 |
| L Isthmus of cingulate cortex | 2.83 | 0.19 | 2.88 | 0.18 | 8.302  | 0.004  | 0.137 |
| L Lateral occipital cortex | 2.72 | 0.13 | 2.75 | 0.13 | 5.689  | 0.017  | 0.113 |
| **L Lateral orbitofrontal cortex** | 2.71 | 0.14 | 2.76 | 0.14 | **17.806**  | **2.97.E-05** | 0.200 |
| **L Lingual gyrus** | 2.86 | 0.16 | 2.92 | 0.15 | **13.862**  | **2.22.E-04** | 0.177 |
| L Medial orbitofrontal cortex | 2.16 | 0.10 | 2.19 | 0.10 | 11.138  | 0.001  | 0.159 |
| L Middle temporal gyrus | 3.49 | 0.23 | 3.56 | 0.22 | 9.625  | 0.002  | 0.147 |
| L Parahippocampal gyrus | 2.87 | 0.18 | 2.93 | 0.16 | 11.497  | 7.60.E-04 | 0.161 |
| L Paracentral lobule | 2.39 | 0.15 | 2.41 | 0.11 | 2.421  | 0.120  | 0.074 |
| **L Pars opercularis** | 4.25 | 0.33 | 4.44 | 0.33 | **45.285**  | **5.29.E-11** | **0.320** |
| L Pars orbitalis | 3.08 | 0.22 | 3.15 | 0.22 | 10.476  | 0.001  | 0.154 |
| **L Pars triangularis** | 3.83 | 0.31 | 4.02 | 0.29 | **56.671**  | **2.91.E-13** | **0.358** |
| L Pericalcarine cortex | 2.93 | 0.18 | 2.97 | 0.18 | 5.971  | 0.015  | 0.116 |
| **L Postcentral gyrus** | 3.56 | 0.23 | 3.63 | 0.18 | **16.949**  | **4.58.E-05** | 0.196 |
| L Posterior cingulate cortex | 2.26 | 0.14 | 2.28 | 0.13 | 2.737  | 0.099  | 0.079 |
| **L Precentral gyrus** | 3.48 | 0.23 | 3.57 | 0.18 | **30.621**  | **5.38.E-08** | **0.263** |
| L Precuneus | 2.98 | 0.19 | 3.03 | 0.17 | 9.975  | 0.002  | 0.150 |
| L Rostral anterior cingulate cortex | 2.06 | 0.11 | 2.10 | 0.10 | 8.715  | 0.003  | 0.140 |
| **L Rostral middle frontal gyrus** | 2.81 | 0.18 | 2.88 | 0.16 | **26.996**  | **3.12.E-07** | 0.247 |
| **L Superior frontal gyrus** | 2.20 | 0.10 | 2.23 | 0.10 | **12.437**  | **4.65.E-04** | 0.168 |
| L Superior parietal cortex | 3.08 | 0.15 | 3.11 | 0.15 | 3.328  | 0.069  | 0.087 |
| **L Superior temporal cortex** | 4.23 | 0.30 | 4.35 | 0.27 | **23.287**  | **1.92.E-06** | 0.229 |
| **L Supramarginal gyrus** | 3.65 | 0.24 | 3.72 | 0.19 | **12.414**  | **4.70.E-04** | 0.167 |
| L Frontal pole | 2.12 | 0.12 | 2.15 | 0.11 | 8.447  | 0.004  | 0.138 |
| L Temporal pole | 2.50 | 0.18 | 2.52 | 0.14 | 0.412  | 0.521  | 0.030 |
| **L Transverse temporal cortex** | 4.84 | 0.38 | 4.99 | 0.34 | **24.137**  | **1.26.E-06** | 0.233 |
| **L Insula** | 4.39 | 0.36 | 4.55 | 0.31 | **30.148**  | **6.76.E-08** | **0.261** |
| ***Right hemisphere*** |  |  |  |  |  |  |  |
| R Caudal anterior cingulate cortex | 1.96 | 0.11 | 1.98 | 0.11 | 5.234  | 0.023  | 0.109 |
| **R Caudal middle frontal gyrus** | 3.16 | 0.19 | 3.24 | 0.19 | **24.405**  | **1.11.E-06** | 0.235 |
| R Cuneus | 3.25 | 0.22 | 3.30 | 0.20 | 7.592  | 0.006  | 0.131 |
| **R Entorhinal cortex** | 2.65 | 0.14 | 2.71 | 0.13 | **19.645**  | **1.18.E-05** | 0.211 |
| R Fusiform gyrus | 2.75 | 0.13 | 2.78 | 0.12 | 5.419  | 0.020  | 0.111 |
| **R Inferior parietal cortex** | 3.35 | 0.18 | 3.41 | 0.17 | **16.694**  | **5.21.E-05** | 0.194 |
| R Inferior temporal gyrus | 2.75 | 0.13 | 2.77 | 0.13 | 2.041  | 0.154  | 0.068 |
| R Isthmus of cingulate cortex | 2.94 | 0.21 | 2.99 | 0.20 | 7.454  | 0.007  | 0.130 |
| R Lateral occipital cortex | 2.74 | 0.13 | 2.77 | 0.13 | 5.853  | 0.016  | 0.115 |
| **R Lateral orbitofrontal cortex** | 2.64 | 0.15 | 2.71 | 0.14 | **25.321**  | **7.07.E-07** | 0.239 |
| R Lingual gyrus | 2.97 | 0.18 | 3.01 | 0.18 | 6.516  | 0.011  | 0.121 |
| **R Medial orbitofrontal cortex** | 2.16 | 0.10 | 2.21 | 0.10 | **21.069**  | **5.78.E-06** | 0.218 |
| R Middle temporal gyrus | 3.43 | 0.21 | 3.46 | 0.20 | 2.919  | 0.088  | 0.081 |
| R Parahippocampal gyrus | 2.89 | 0.18 | 2.94 | 0.17 | 7.707  | 0.006  | 0.132 |
| R Paracentral lobule | 2.39 | 0.13 | 2.41 | 0.11 | 5.108  | 0.024  | 0.107 |
| **R Pars opercularis** | 4.28 | 0.35 | 4.46 | 0.36 | **33.715**  | **1.22.E-08** | **0.276** |
| R Pars orbitalis | 3.07 | 0.25 | 3.10 | 0.23 | 1.263  | 0.262  | 0.053 |
| **R Pars triangularis** | 3.86 | 0.31 | 3.99 | 0.31 | **20.433**  | **7.93.E-06** | 0.215 |
| R Pericalcarine cortex | 3.09 | 0.21 | 3.15 | 0.20 | 8.679  | 0.003  | 0.140 |
| **R Postcentral gyrus** | 3.51 | 0.21 | 3.59 | 0.19 | **21.992**  | **3.65.E-06** | 0.223 |
| R Posterior cingulate cortex | 2.25 | 0.15 | 2.28 | 0.13 | 4.471  | 0.035  | 0.100 |
| **R Precentral gyrus** | 3.44 | 0.20 | 3.52 | 0.18 | **27.115**  | **2.94.E-07** | 0.247 |
| R Precuneus | 3.12 | 0.21 | 3.19 | 0.19 | 11.117  | 0.001  | 0.158 |
| **R Rostral anterior cingulate cortex** | 2.10 | 0.11 | 2.14 | 0.11 | **12.228**  | **5.18.E-04** | 0.166 |
| **R Rostral middle frontal gyrus** | 2.79 | 0.17 | 2.87 | 0.17 | **22.686**  | **2.59.E-06** | 0.226 |
| R Superior frontal gyrus | 2.25 | 0.10 | 2.28 | 0.10 | 11.048  | 9.61.E-04 | 0.158 |
| **R Superior parietal cortex** | 3.05 | 0.15 | 3.10 | 0.14 | **14.145**  | **1.92.E-04** | 0.179 |
| **R Superior temporal cortex** | 4.20 | 0.29 | 4.30 | 0.28 | **16.557**  | **5.59.E-05** | 0.193 |
| **R Supramarginal gyrus** | 3.64 | 0.22 | 3.71 | 0.20 | **15.181**  | **1.13.E-04** | 0.185 |
| R Frontal pole | 2.15 | 0.12 | 2.18 | 0.11 | 6.254  | 0.013  | 0.119 |
| **R Temporal pole** | 2.48 | 0.14 | 2.54 | 0.14 | **19.593**  | **1.21.E-05** | 0.210 |
| **R Transverse temporal cortex** | 4.86 | 0.39 | 4.98 | 0.35 | **14.215**  | **1.85.E-04** | 0.179 |
| **R Insula** | 4.37 | 0.33 | 4.49 | 0.31 | **16.343**  | **6.23.E-05** | 0.192 |

F and P values were obtained using one-way analysis of covariance (ANCOVA) with adjustments for age, sex, years of education, and total intracranial cavity volume as covariates.

Bonferroni correction was applied; P < 0.05/66 = 0.000758.

Significant group differences are presented in a bold face.

MDD, major depressive disorder; HC, healthy control; SD, standard deviation.

**Table S3. Model 2: Comparison of local gyrification index between patients with major depressive disorders and healthy controls controlling for equivalent doses of antidepressant and antipsychotics**

|  |  |  |  |
| --- | --- | --- | --- |
| **Cortical regions** | **MDD (n = 234)** | **HC (n = 215)** | **MDD vs. HC** |
| **mean** | **SD** | **mean** | **SD** | **F (1, 442)** | **P-value** | **Cohen's f** |
| ***Left hemisphere*** |  |  |  |  |  |  |  |
| L Caudal anterior cingulate cortex | 1.91 | 0.11 | 1.93 | 0.11 | 3.534  | 0.061  | 0.089 |
| **L Caudal middle frontal gyrus** | 3.19 | 0.21 | 3.27 | 0.19 | **18.917**  | **1.70.E-05** | 0.207 |
| L Cuneus | 3.06 | 0.20 | 3.10 | 0.19 | 6.119  | 0.014  | 0.118 |
| L Entorhinal cortex | 2.64 | 0.13 | 2.67 | 0.13 | 9.376  | 0.002  | 0.146 |
| **L Fusiform gyrus** | 2.78 | 0.12 | 2.81 | 0.11 | **11.777**  | **6.56.E-04** | 0.163 |
| L Inferior parietal cortex | 3.36 | 0.19 | 3.41 | 0.17 | **13.733**  | **2.37.E-04** | 0.176 |
| L Inferior temporal gyrus | 2.82 | 0.12 | 2.84 | 0.12 | 3.988  | 0.046  | 0.095 |
| L Isthmus of cingulate cortex | 2.83 | 0.19 | 2.88 | 0.18 | 8.961  | 0.003  | 0.142 |
| L Lateral occipital cortex | 2.72 | 0.13 | 2.75 | 0.13 | 7.025  | 0.008  | 0.126 |
| **L Lateral orbitofrontal cortex** | 2.71 | 0.14 | 2.76 | 0.14 | **11.563**  | **7.34.E-04** | 0.162 |
| L Lingual gyrus | 2.86 | 0.16 | 2.92 | 0.15 | 8.415  | 0.004  | 0.138 |
| **L Medial orbitofrontal cortex** | 2.16 | 0.10 | 2.19 | 0.10 | **13.096**  | **3.30.E-04** | 0.172 |
| L Middle temporal gyrus | 3.49 | 0.23 | 3.56 | 0.22 | 10.508  | 0.001  | 0.154 |
| L Parahippocampal gyrus | 2.87 | 0.18 | 2.93 | 0.16 | 9.206  | 0.003  | 0.144 |
| L Paracentral lobule | 2.39 | 0.15 | 2.41 | 0.11 | 1.050  | 0.306  | 0.049 |
| **L Pars opercularis** | 4.25 | 0.33 | 4.44 | 0.33 | **31.793**  | **3.06.E-08** | 0.268 |
| L Pars orbitalis | 3.08 | 0.22 | 3.15 | 0.22 | 7.780  | 0.006  | 0.133 |
| **L Pars triangularis** | 3.83 | 0.31 | 4.02 | 0.29 | **38.140**  | **1.49.E-09** | 0.294 |
| L Pericalcarine cortex | 2.93 | 0.18 | 2.97 | 0.18 | 4.941  | 0.027  | 0.106 |
| **L Postcentral gyrus** | 3.56 | 0.23 | 3.63 | 0.18 | **20.492**  | **7.71.E-06** | 0.215 |
| L Posterior cingulate cortex | 2.26 | 0.14 | 2.28 | 0.13 | 3.159  | 0.076  | 0.085 |
| **L Precentral gyrus** | 3.48 | 0.23 | 3.57 | 0.18 | **28.207**  | **1.73.E-07** | 0.253 |
| L Precuneus | 2.98 | 0.19 | 3.03 | 0.17 | **13.986**  | **2.08.E-04** | 0.178 |
| L Rostral anterior cingulate cortex | 2.06 | 0.11 | 2.10 | 0.10 | 8.456  | 0.004  | 0.138 |
| **L Rostral middle frontal gyrus** | 2.81 | 0.18 | 2.88 | 0.16 | **29.114**  | **1.11.E-07** | 0.257 |
| L Superior frontal gyrus | 2.20 | 0.10 | 2.23 | 0.10 | 10.124  | 0.002  | 0.151 |
| L Superior parietal cortex | 3.08 | 0.15 | 3.11 | 0.15 | 2.494  | 0.115  | 0.075 |
| **L Superior temporal cortex** | 4.23 | 0.30 | 4.35 | 0.27 | **21.670**  | **4.29.E-06** | 0.221 |
| **L Supramarginal gyrus** | 3.65 | 0.24 | 3.72 | 0.19 | **16.239**  | **6.57.E-05** | 0.192 |
| L Frontal pole | 2.12 | 0.12 | 2.15 | 0.11 | 8.528  | 0.004  | 0.139 |
| L Temporal pole | 2.50 | 0.18 | 2.52 | 0.14 | 0.287  | 0.593  | 0.025 |
| **L Transverse temporal cortex** | 4.84 | 0.38 | 4.99 | 0.34 | **18.368**  | **2.24.E-05** | 0.204 |
| **L Insula** | 4.39 | 0.36 | 4.55 | 0.31 | **23.608**  | **1.64.E-06** | 0.231 |
| ***Right hemisphere*** |  |  |  |  |  |  |  |
| R Caudal anterior cingulate cortex | 1.96 | 0.11 | 1.98 | 0.11 | 4.420  | 0.036  | 0.100 |
| **R Caudal middle frontal gyrus** | 3.16 | 0.19 | 3.24 | 0.19 | **24.688**  | **9.65.E-07** | 0.236 |
| R Cuneus | 3.25 | 0.22 | 3.30 | 0.20 | 9.734  | 0.002  | 0.148 |
| **R Entorhinal cortex** | 2.65 | 0.14 | 2.71 | 0.13 | **17.662**  | **3.19.E-05** | 0.200 |
| R Fusiform gyrus | 2.75 | 0.13 | 2.78 | 0.12 | 7.941  | 0.005  | 0.134 |
| **R Inferior parietal cortex** | 3.35 | 0.18 | 3.41 | 0.17 | **20.747**  | **6.79.E-06** | 0.217 |
| R Inferior temporal gyrus | 2.75 | 0.13 | 2.77 | 0.13 | 8.383  | 0.004  | 0.138 |
| R Isthmus of cingulate cortex | 2.94 | 0.21 | 2.99 | 0.20 | 4.952  | 0.027  | 0.106 |
| R Lateral occipital cortex | 2.74 | 0.13 | 2.77 | 0.13 | **13.719**  | **2.39.E-04** | 0.176 |
| **R Lateral orbitofrontal cortex** | 2.64 | 0.15 | 2.71 | 0.14 | **26.199**  | **4.60.E-07** | 0.243 |
| R Lingual gyrus | 2.97 | 0.18 | 3.01 | 0.18 | 5.312  | 0.022  | 0.110 |
| **R Medial orbitofrontal cortex** | 2.16 | 0.10 | 2.21 | 0.10 | **23.134**  | **2.08.E-06** | 0.229 |
| R Middle temporal gyrus | 3.43 | 0.21 | 3.46 | 0.20 | 6.329  | 0.012  | 0.120 |
| R Parahippocampal gyrus | 2.89 | 0.18 | 2.94 | 0.17 | 5.446  | 0.020  | 0.111 |
| R Paracentral lobule | 2.39 | 0.13 | 2.41 | 0.11 | 5.121  | 0.024  | 0.108 |
| **R Pars opercularis** | 4.28 | 0.35 | 4.46 | 0.36 | **23.068**  | **2.14.E-06** | 0.228 |
| R Pars orbitalis | 3.07 | 0.25 | 3.10 | 0.23 | 4.626  | 0.032  | 0.102 |
| **R Pars triangularis** | 3.86 | 0.31 | 3.99 | 0.31 | **17.146**  | **4.15.E-05** | 0.197 |
| R Pericalcarine cortex | 3.09 | 0.21 | 3.15 | 0.20 | 10.037  | 0.002  | 0.151 |
| **R Postcentral gyrus** | 3.51 | 0.21 | 3.59 | 0.19 | **25.917**  | **5.28.E-07** | 0.242 |
| R Posterior cingulate cortex | 2.25 | 0.15 | 2.28 | 0.13 | 3.472  | 0.063  | 0.089 |
| **R Precentral gyrus** | 3.44 | 0.20 | 3.52 | 0.18 | **26.890**  | **3.29.E-07** | 0.247 |
| **R Precuneus** | 3.12 | 0.21 | 3.19 | 0.19 | **11.907**  | **6.13.E-04** | 0.164 |
| R Rostral anterior cingulate cortex | 2.10 | 0.11 | 2.14 | 0.11 | 11.288  | 8.48.E-04 | 0.160 |
| **R Rostral middle frontal gyrus** | 2.79 | 0.17 | 2.87 | 0.17 | **17.804**  | **2.97.E-05** | 0.201 |
| **R Superior frontal gyrus** | 2.25 | 0.10 | 2.28 | 0.10 | **12.868**  | **3.71.E-04** | 0.171 |
| **R Superior parietal cortex** | 3.05 | 0.15 | 3.10 | 0.14 | **15.286**  | **1.07.E-04** | 0.186 |
| **R Superior temporal cortex** | 4.20 | 0.29 | 4.30 | 0.28 | **19.704**  | **1.14.E-05** | 0.211 |
| **R Supramarginal gyrus** | 3.64 | 0.22 | 3.71 | 0.20 | **19.583**  | **1.22.E-05** | 0.210 |
| R Frontal pole | 2.15 | 0.12 | 2.18 | 0.11 | 6.859  | 0.009  | 0.125 |
| **R Temporal pole** | 2.48 | 0.14 | 2.54 | 0.14 | **22.670**  | **2.61.E-06** | 0.226 |
| **R Transverse temporal cortex** | 4.86 | 0.39 | 4.98 | 0.35 | **19.888**  | **1.04.E-05** | 0.212 |
| **R Insula** | 4.37 | 0.33 | 4.49 | 0.31 | **18.874**  | **1.73.E-05** | 0.207 |

F and P values were obtained using one-way analysis of covariance (ANCOVA) with adjustment for age, sex, education years, and equivalents of antidepressants and antipsychotics (respectively).

Bonferroni correction was applied; P < 0.05/66 = 0.000758.

Significant group differences are presented in a bold face.

MDD, major depressive disorder; HC, healthy control; SD, standard deviation.

**Table S4. Model 3: Comparison of local gyrification index between patients with major depressive disorders and healthy controls controlling for total intracranial cavity volume and equivalent doses of antidepressant and antipsychotics**

|  |  |  |  |
| --- | --- | --- | --- |
| **Cortical regions** | **MDD (n = 234)** | **HC (n = 215)** | **MDD vs. HC** |
| **mean** | **SD** | **mean** | **SD** | **F (1, 441)** | **P-value** | **Cohen's f** |
| ***Left hemisphere*** |  |  |  |  |  |  |  |
| L Caudal anterior cingulate cortex | 1.91 | 0.11 | 1.93 | 0.11 | 2.741  | 0.099  | 0.079 |
| **L Caudal middle frontal gyrus** | 3.19 | 0.21 | 3.27 | 0.19 | **17.682**  | **3.16.E-05** | 0.200 |
| L Cuneus | 3.06 | 0.20 | 3.10 | 0.19 | 5.165  | 0.024  | 0.108 |
| L Entorhinal cortex | 2.64 | 0.13 | 2.67 | 0.13 | 8.176  | 0.004  | 0.136 |
| L Fusiform gyrus | 2.78 | 0.12 | 2.81 | 0.11 | 10.551  | 0.001  | 0.155 |
| **L Inferior parietal cortex** | 3.36 | 0.19 | 3.41 | 0.17 | **12.482**  | **4.54.E-04** | 0.168 |
| L Inferior temporal gyrus | 2.82 | 0.12 | 2.84 | 0.12 | 3.486  | 0.063  | 0.089 |
| L Isthmus of cingulate cortex | 2.83 | 0.19 | 2.88 | 0.18 | 8.095  | 0.005  | 0.135 |
| L Lateral occipital cortex | 2.72 | 0.13 | 2.75 | 0.13 | 6.552  | 0.011  | 0.122 |
| L Lateral orbitofrontal cortex | 2.71 | 0.14 | 2.76 | 0.14 | 10.449  | 0.001  | 0.154 |
| L Lingual gyrus | 2.86 | 0.16 | 2.92 | 0.15 | 7.155  | 0.008  | 0.127 |
| **L Medial orbitofrontal cortex** | 2.16 | 0.10 | 2.19 | 0.10 | **11.964**  | **5.95.E-04** | 0.165 |
| L Middle temporal gyrus | 3.49 | 0.23 | 3.56 | 0.22 | 9.276  | 0.002  | 0.145 |
| L Parahippocampal gyrus | 2.87 | 0.18 | 2.93 | 0.16 | 8.116  | 0.005  | 0.136 |
| L Paracentral lobule | 2.39 | 0.15 | 2.41 | 0.11 | 0.741  | 0.390  | 0.041 |
| **L Pars opercularis** | 4.25 | 0.33 | 4.44 | 0.33 | **30.302**  | **6.29.E-08** | 0.262 |
| L Pars orbitalis | 3.08 | 0.22 | 3.15 | 0.22 | 7.514  | 0.006  | 0.131 |
| **L Pars triangularis** | 3.83 | 0.31 | 4.02 | 0.29 | **36.927**  | **2.65.E-09** | 0.289 |
| L Pericalcarine cortex | 2.93 | 0.18 | 2.97 | 0.18 | 3.932  | 0.048  | 0.094 |
| **L Postcentral gyrus** | 3.56 | 0.23 | 3.63 | 0.18 | **19.118**  | **1.53.E-05** | 0.208 |
| L Posterior cingulate cortex | 2.26 | 0.14 | 2.28 | 0.13 | 2.453  | 0.118  | 0.075 |
| **L Precentral gyrus** | 3.48 | 0.23 | 3.57 | 0.18 | **26.733**  | **3.55.E-07** | 0.246 |
| **L Precuneus** | 2.98 | 0.19 | 3.03 | 0.17 | **12.718**  | **4.02.E-04** | 0.170 |
| L Rostral anterior cingulate cortex | 2.06 | 0.11 | 2.10 | 0.10 | 7.337  | 0.007  | 0.129 |
| **L Rostral middle frontal gyrus** | 2.81 | 0.18 | 2.88 | 0.16 | **27.637**  | **2.29.E-07** | 0.250 |
| L Superior frontal gyrus | 2.20 | 0.10 | 2.23 | 0.10 | 8.945  | 0.003  | 0.142 |
| L Superior parietal cortex | 3.08 | 0.15 | 3.11 | 0.15 | 2.040  | 0.154  | 0.068 |
| **L Superior temporal cortex** | 4.23 | 0.30 | 4.35 | 0.27 | **20.276**  | **8.59.E-06** | 0.214 |
| **L Supramarginal gyrus** | 3.65 | 0.24 | 3.72 | 0.19 | **14.961**  | **1.26.E-04** | 0.184 |
| L Frontal pole | 2.12 | 0.12 | 2.15 | 0.11 | 7.602  | 0.006  | 0.131 |
| L Temporal pole | 2.50 | 0.18 | 2.52 | 0.14 | 0.122  | 0.727  | 0.017 |
| **L Transverse temporal cortex** | 4.84 | 0.38 | 4.99 | 0.34 | **17.000**  | **4.47.E-05** | 0.196 |
| **L Insula** | 4.39 | 0.36 | 4.55 | 0.31 | **22.190**  | **3.31.E-06** | 0.224 |
| ***Right hemisphere*** |  |  |  |  |  |  |  |
| R Caudal anterior cingulate cortex | 1.96 | 0.11 | 1.98 | 0.11 | 3.428  | 0.065  | 0.088 |
| **R Caudal middle frontal gyrus** | 3.16 | 0.19 | 3.24 | 0.19 | **23.454**  | **1.77.E-06** | 0.231 |
| R Cuneus | 3.25 | 0.22 | 3.30 | 0.20 | 8.603  | 0.004  | 0.140 |
| **R Entorhinal cortex** | 2.65 | 0.14 | 2.71 | 0.13 | **16.648**  | **5.34.E-05** | 0.194 |
| R Fusiform gyrus | 2.75 | 0.13 | 2.78 | 0.12 | 6.973  | 0.009  | 0.126 |
| **R Inferior parietal cortex** | 3.35 | 0.18 | 3.41 | 0.17 | **19.311**  | **1.39.E-05** | 0.209 |
| R Inferior temporal gyrus | 2.75 | 0.13 | 2.77 | 0.13 | 7.622  | 0.006  | 0.131 |
| R Isthmus of cingulate cortex | 2.94 | 0.21 | 2.99 | 0.20 | 4.409  | 0.036  | 0.100 |
| **R Lateral occipital cortex** | 2.74 | 0.13 | 2.77 | 0.13 | **12.688**  | **4.08.E-04** | 0.170 |
| **R Lateral orbitofrontal cortex** | 2.64 | 0.15 | 2.71 | 0.14 | **24.740**  | **9.42.E-07** | 0.237 |
| R Lingual gyrus | 2.97 | 0.18 | 3.01 | 0.18 | 4.435  | 0.036  | 0.100 |
| **R Medial orbitofrontal cortex** | 2.16 | 0.10 | 2.21 | 0.10 | **21.742**  | **4.14.E-06** | 0.222 |
| R Middle temporal gyrus | 3.43 | 0.21 | 3.46 | 0.20 | 5.249  | 0.022  | 0.109 |
| R Parahippocampal gyrus | 2.89 | 0.18 | 2.94 | 0.17 | 4.792  | 0.029  | 0.104 |
| R Paracentral lobule | 2.39 | 0.13 | 2.41 | 0.11 | 4.364  | 0.037  | 0.099 |
| **R Pars opercularis** | 4.28 | 0.35 | 4.46 | 0.36 | **21.662**  | **4.31.E-06** | 0.222 |
| R Pars orbitalis | 3.07 | 0.25 | 3.10 | 0.23 | 3.958  | 0.047  | 0.095 |
| **R Pars triangularis** | 3.86 | 0.31 | 3.99 | 0.31 | **16.049**  | **7.24.E-05** | 0.191 |
| R Pericalcarine cortex | 3.09 | 0.21 | 3.15 | 0.20 | 8.882  | 0.003  | 0.142 |
| **R Postcentral gyrus** | 3.51 | 0.21 | 3.59 | 0.19 | **24.547**  | **1.04.E-06** | 0.236 |
| R Posterior cingulate cortex | 2.25 | 0.15 | 2.28 | 0.13 | 2.842  | 0.093  | 0.080 |
| **R Precentral gyrus** | 3.44 | 0.20 | 3.52 | 0.18 | **25.473**  | **6.57.E-07** | 0.240 |
| R Precuneus | 3.12 | 0.21 | 3.19 | 0.19 | 10.588  | 0.001  | 0.155 |
| R Rostral anterior cingulate cortex | 2.10 | 0.11 | 2.14 | 0.11 | 9.968  | 0.002  | 0.150 |
| **R Rostral middle frontal gyrus** | 2.79 | 0.17 | 2.87 | 0.17 | **16.395**  | **6.07.E-05** | 0.193 |
| **R Superior frontal gyrus** | 2.25 | 0.10 | 2.28 | 0.10 | **11.681**  | **6.90.E-04** | 0.163 |
| **R Superior parietal cortex** | 3.05 | 0.15 | 3.10 | 0.14 | **14.071**  | **2.00.E-04** | 0.179 |
| **R Superior temporal cortex** | 4.20 | 0.29 | 4.30 | 0.28 | **18.465**  | **2.13.E-05** | 0.205 |
| **R Supramarginal gyrus** | 3.64 | 0.22 | 3.71 | 0.20 | **18.153**  | **2.49.E-05** | 0.203 |
| R Frontal pole | 2.15 | 0.12 | 2.18 | 0.11 | 6.013  | 0.015  | 0.117 |
| **R Temporal pole** | 2.48 | 0.14 | 2.54 | 0.14 | **21.400**  | **4.91.E-06** | 0.220 |
| **R Transverse temporal cortex** | 4.86 | 0.39 | 4.98 | 0.35 | **18.820**  | **1.78.E-05** | 0.207 |
| **R Insula** | 4.37 | 0.33 | 4.49 | 0.31 | **17.449**  | **3.56.E-05** | 0.199 |

F and P values were obtained using one-way analysis of covariance (ANCOVA) with adjustment for age, sex, years of education, total intracranial cavity volume, and equivalents of antidepressants and antipsychotics (respectively).

Bonferroni correction was applied; P < 0.05/66 = 0.000758.

Significant group differences are presented in a bold face.

MDD, major depressive disorder; HC, healthy control; SD, standard deviation.

**Table S5. Comparison of the local gyrification index between patients with first-episode and recurrent MDD**

|  |  |  |  |
| --- | --- | --- | --- |
| **Cortical regions** | **F-MDD (n = 104)** | **RC-MDD (n = 130)** | **F-MDD vs. RC-MDD** |
| **Mean** | **SD** | **Mean** | **SD** | **F (1, 227)** | **P-value** |
| ***Left hemisphere*** |  |  |  |  |  |  |
| Caudal anterior cingulate cortex | 1.90 | 0.10 | 1.91 | 0.12 | 0.303 | 0.583 |
| Caudal middle frontal gyrus | 3.19 | 0.22 | 3.19 | 0.20 | 2.490 | 0.116 |
| Cuneus | 3.02 | 0.21 | 3.09 | 0.19 | 3.810 | 0.052 |
| Entorhinal cortex | 2.62 | 0.12 | 2.65 | 0.13 | 2.823 | 0.094 |
| Fusiform gyrus | 2.75 | 0.11 | 2.80 | 0.12 | 5.513 | 0.020 |
| Inferior parietal cortex | 3.32 | 0.19 | 3.39 | 0.19 | 3.083 | 0.080 |
| Inferior temporal gyrus | 2.80 | 0.11 | 2.84 | 0.13 | 2.827 | 0.094 |
| Isthmus of cingulate cortex | 2.79 | 0.19 | 2.86 | 0.18 | 4.092 | 0.044 |
| Lateral occipital cortex | 2.69 | 0.12 | 2.74 | 0.14 | 3.929 | 0.049 |
| Lateral orbitofrontal cortex | 2.69 | 0.14 | 2.72 | 0.14 | 0.464 | 0.496 |
| Lingual gyrus | 2.83 | 0.16 | 2.89 | 0.16 | 3.786 | 0.053 |
| Medial orbitofrontal cortex | 2.15 | 0.09 | 2.17 | 0.10 | 0.450 | 0.503 |
| Middle temporal gyrus | 3.45 | 0.21 | 3.53 | 0.23 | 2.954 | 0.087 |
| Parahippocampal gyrus | 2.84 | 0.19 | 2.90 | 0.16 | 2.298 | 0.131 |
| Paracentral lobule | 2.39 | 0.18 | 2.39 | 0.11 | 0.063 | 0.801 |
| Pars opercularis | 4.21 | 0.35 | 4.28 | 0.32 | 0.314 | 0.576 |
| Pars orbitalis | 3.07 | 0.22 | 3.09 | 0.22 | 0.324 | 0.570 |
| Pars triangularis | 3.78 | 0.32 | 3.87 | 0.29 | 2.137 | 0.145 |
| Pericalcarine cortex | 2.89 | 0.18 | 2.95 | 0.18 | 3.323 | 0.070 |
| Postcentral gyrus | 3.53 | 0.26 | 3.58 | 0.21 | 0.100 | 0.752 |
| Posterior cingulate cortex | 2.24 | 0.14 | 2.27 | 0.14 | 0.389 | 0.534 |
| Precentral gyrus | 3.45 | 0.26 | 3.50 | 0.21 | 0.348 | 0.556 |
| Precuneus | 2.94 | 0.19 | 3.01 | 0.18 | 4.381 | 0.037 |
| Rostral anterior cingulate cortex | 2.06 | 0.10 | 2.07 | 0.11 | 0.275 | 0.600 |
| Rostral middle frontal gyrus | 2.78 | 0.18 | 2.83 | 0.17 | 2.211 | 0.138 |
| Superior frontal gyrus | 2.20 | 0.11 | 2.20 | 0.10 | 2.041 | 0.155 |
| Superior parietal cortex | 3.07 | 0.14 | 3.09 | 0.16 | 0.122 | 0.727 |
| Superior temporal cortex | 4.18 | 0.29 | 4.27 | 0.30 | 1.302 | 0.255 |
| Supramarginal gyrus | 3.62 | 0.26 | 3.68 | 0.21 | 0.585 | 0.445 |
| Frontal pole | 2.12 | 0.12 | 2.12 | 0.11 | 0.199 | 0.656 |
| Temporal pole | 2.50 | 0.22 | 2.50 | 0.14 | 0.000 | 0.989 |
| Transverse temporal cortex | 4.78 | 0.36 | 4.89 | 0.38 | 1.302 | 0.255 |
| Insula | 4.33 | 0.36 | 4.43 | 0.34 | 1.456 | 0.229 |
| *Right hemisphere* |  |  |  |  |  |  |
| Caudal anterior cingulate cortex | 1.95 | 0.11 | 1.97 | 0.11 | 0.069 | 0.793 |
| Caudal middle frontal gyrus | 3.15 | 0.18 | 3.17 | 0.20 | 0.590 | 0.443 |
| Cuneus | 3.20 | 0.21 | 3.29 | 0.21 | 6.218 | 0.013 |
| Entorhinal cortex | 2.62 | 0.13 | 2.67 | 0.13 | 5.674 | 0.018 |
| Fusiform gyrus | 2.71 | 0.12 | 2.78 | 0.12 | 9.553 | 0.002 |
| Inferior parietal cortex | 3.31 | 0.18 | 3.38 | 0.18 | 3.630 | 0.058 |
| Inferior temporal gyrus | 2.72 | 0.12 | 2.77 | 0.13 | 5.090 | 0.025 |
| Isthmus of cingulate cortex | 2.90 | 0.20 | 2.96 | 0.21 | 3.847 | 0.051 |
| **Lateral occipital cortex** | 2.70 | 0.12 | 2.77 | 0.12 | **17.702** | **3.72 × 10-5** |
| Lateral orbitofrontal cortex | 2.62 | 0.15 | 2.66 | 0.14 | 0.902 | 0.343 |
| Lingual gyrus | 2.92 | 0.19 | 3.00 | 0.17 | 7.735 | 0.006 |
| Medial orbitofrontal cortex | 2.14 | 0.10 | 2.18 | 0.10 | 5.312 | 0.022 |
| Middle temporal gyrus | 3.40 | 0.19 | 3.45 | 0.22 | 0.970 | 0.326 |
| Parahippocampal gyrus | 2.86 | 0.18 | 2.92 | 0.17 | 4.668 | 0.032 |
| Paracentral lobule | 2.39 | 0.13 | 2.39 | 0.14 | 0.383 | 0.537 |
| Pars opercularis | 4.24 | 0.34 | 4.32 | 0.36 | 0.768 | 0.382 |
| Pars orbitalis | 3.05 | 0.25 | 3.08 | 0.24 | 0.027 | 0.870 |
| Pars triangularis | 3.83 | 0.33 | 3.88 | 0.29 | 0.175 | 0.676 |
| Pericalcarine cortex | 3.05 | 0.22 | 3.13 | 0.20 | 5.476 | 0.020 |
| Postcentral gyrus | 3.50 | 0.20 | 3.52 | 0.23 | 0.204 | 0.652 |
| Posterior cingulate cortex | 2.24 | 0.14 | 2.26 | 0.15 | 0.199 | 0.656 |
| Precentral gyrus | 3.42 | 0.19 | 3.46 | 0.21 | 0.055 | 0.815 |
| Precuneus | 3.09 | 0.20 | 3.15 | 0.21 | 2.989 | 0.085 |
| Rostral anterior cingulate cortex | 2.08 | 0.11 | 2.12 | 0.11 | 2.370 | 0.125 |
| Rostral middle frontal gyrus | 2.78 | 0.17 | 2.81 | 0.18 | 0.006 | 0.940 |
| Superior frontal gyrus | 2.24 | 0.10 | 2.25 | 0.11 | 1.053 | 0.306 |
| Superior parietal cortex | 3.03 | 0.14 | 3.07 | 0.16 | 0.367 | 0.545 |
| Superior temporal cortex | 4.16 | 0.27 | 4.24 | 0.31 | 0.947 | 0.331 |
| Supramarginal gyrus | 3.61 | 0.20 | 3.67 | 0.23 | 0.450 | 0.503 |
| Frontal pole | 2.14 | 0.11 | 2.16 | 0.12 | 0.002 | 0.962 |
| Temporal pole | 2.45 | 0.14 | 2.49 | 0.15 | 1.910 | 0.168 |
| Transverse temporal cortex | 4.79 | 0.34 | 4.91 | 0.41 | 1.443 | 0.231 |
| Insula | 4.30 | 0.33 | 4.42 | 0.32 | 2.993 | 0.085 |

F and P values were obtained using one-way analysis of covariance (ANCOVA), with age, sex, education years, HDRS score, and medication as covariates.

Bonferroni correction was applied; P < 0.05/66 = 0.000758.

Significant group differences are presented in a bold face.

F-MDD, first episode of major depressive disorder; R-MDD, recurrent major depressive disorder; SD, standard deviation.

**Table S6. Comparison of the local gyrification index between remitted and non-remitted patients with MDD**

|  |  |  |  |
| --- | --- | --- | --- |
| **Cortical regions** | **R-MDD (n = 22)** | **NR-MDD (n = 212)** | **R-MDD vs. NR-MDD** |
| **Mean** | **SD** | **Mean** | **SD** | **F (1, 227)** | **P-value** |
| ***Left hemisphere*** |  |  |  |  |  |  |
| Caudal anterior cingulate cortex | 1.93 | 0.11 | 1.90 | 0.11 | 0.407 | 0.524 |
| Caudal middle frontal gyrus | 3.20 | 0.24 | 3.19 | 0.21 | 0.765 | 0.383 |
| Cuneus | 3.11 | 0.21 | 3.05 | 0.20 | 0.458 | 0.499 |
| Entorhinal cortex | 2.68 | 0.13 | 2.63 | 0.13 | 0.951 | 0.331 |
| Fusiform gyrus | 2.82 | 0.10 | 2.77 | 0.12 | 1.784 | 0.183 |
| Inferior parietal cortex | 3.42 | 0.15 | 3.35 | 0.20 | 1.768 | 0.185 |
| Inferior temporal gyrus | 2.83 | 0.12 | 2.82 | 0.12 | 0.244 | 0.622 |
| Isthmus of cingulate cortex | 2.88 | 0.15 | 2.83 | 0.19 | 0.185 | 0.667 |
| Lateral occipital cortex | 2.77 | 0.16 | 2.71 | 0.13 | 3.703 | 0.056 |
| Lateral orbitofrontal cortex | 2.71 | 0.12 | 2.71 | 0.14 | 0.122 | 0.728 |
| Lingual gyrus | 2.90 | 0.15 | 2.86 | 0.16 | 0.450 | 0.503 |
| Medial orbitofrontal cortex | 2.18 | 0.10 | 2.16 | 0.10 | 0.887 | 0.347 |
| Middle temporal gyrus | 3.52 | 0.27 | 3.49 | 0.22 | 0.144 | 0.705 |
| Parahippocampal gyrus | 2.95 | 0.14 | 2.87 | 0.18 | 2.192 | 0.140 |
| Paracentral lobule | 2.40 | 0.08 | 2.39 | 0.15 | 0.227 | 0.634 |
| Pars opercularis | 4.34 | 0.37 | 4.24 | 0.33 | 2.585 | 0.109 |
| Pars orbitalis | 3.11 | 0.18 | 3.08 | 0.22 | 0.878 | 0.350 |
| Pars triangularis | 3.88 | 0.29 | 3.82 | 0.31 | 1.137 | 0.287 |
| Pericalcarine cortex | 2.97 | 0.20 | 2.92 | 0.18 | 0.255 | 0.614 |
| Postcentral gyrus | 3.58 | 0.22 | 3.56 | 0.24 | 0.419 | 0.518 |
| Posterior cingulate cortex | 2.29 | 0.11 | 2.25 | 0.14 | 0.361 | 0.548 |
| Precentral gyrus | 3.51 | 0.23 | 3.48 | 0.23 | 0.863 | 0.354 |
| Precuneus | 3.03 | 0.19 | 2.97 | 0.19 | 0.426 | 0.515 |
| Rostral anterior cingulate cortex | 2.07 | 0.11 | 2.06 | 0.11 | 0.007 | 0.935 |
| Rostral middle frontal gyrus | 2.83 | 0.16 | 2.80 | 0.18 | 0.551 | 0.459 |
| Superior frontal gyrus | 2.21 | 0.11 | 2.20 | 0.10 | 0.840 | 0.360 |
| Superior parietal cortex | 3.09 | 0.13 | 3.08 | 0.15 | 0.214 | 0.644 |
| Superior temporal cortex | 4.26 | 0.38 | 4.23 | 0.29 | 0.429 | 0.513 |
| Supramarginal gyrus | 3.69 | 0.25 | 3.65 | 0.24 | 0.593 | 0.442 |
| Frontal pole | 2.10 | 0.14 | 2.12 | 0.12 | 0.603 | 0.438 |
| Temporal pole | 2.46 | 0.14 | 2.51 | 0.18 | 0.939 | 0.334 |
| Transverse temporal cortex | 4.90 | 0.52 | 4.84 | 0.36 | 0.815 | 0.367 |
| Insula | 4.43 | 0.40 | 4.39 | 0.35 | 0.445 | 0.506 |
| *Right hemisphere* |  |  |  |  |  |  |
| Caudal anterior cingulate cortex | 1.96 | 0.11 | 1.96 | 0.11 | 0.112 | 0.738 |
| Caudal middle frontal gyrus | 3.16 | 0.22 | 3.16 | 0.19 | 0.137 | 0.711 |
| Cuneus | 3.31 | 0.19 | 3.24 | 0.22 | 0.879 | 0.350 |
| Entorhinal cortex | 2.69 | 0.10 | 2.65 | 0.14 | 0.330 | 0.566 |
| Fusiform gyrus | 2.79 | 0.07 | 2.74 | 0.13 | 1.078 | 0.300 |
| Inferior parietal cortex | 3.39 | 0.14 | 3.34 | 0.19 | 0.616 | 0.433 |
| Inferior temporal gyrus | 2.79 | 0.08 | 2.75 | 0.13 | 1.985 | 0.160 |
| Isthmus of cingulate cortex | 2.91 | 0.17 | 2.94 | 0.21 | 1.311 | 0.253 |
| Lateral occipital cortex | 2.80 | 0.13 | 2.73 | 0.12 | 4.366 | 0.038 |
| Lateral orbitofrontal cortex | 2.65 | 0.15 | 2.64 | 0.15 | 0.062 | 0.804 |
| Lingual gyrus | 3.00 | 0.16 | 2.96 | 0.18 | 0.015 | 0.904 |
| Medial orbitofrontal cortex | 2.16 | 0.12 | 2.16 | 0.10 | 0.236 | 0.627 |
| Middle temporal gyrus | 3.47 | 0.25 | 3.42 | 0.21 | 0.956 | 0.329 |
| Parahippocampal gyrus | 2.96 | 0.14 | 2.88 | 0.18 | 2.156 | 0.143 |
| Paracentral lobule | 2.40 | 0.12 | 2.39 | 0.13 | 0.314 | 0.576 |
| Pars opercularis | 4.33 | 0.42 | 4.28 | 0.34 | 0.654 | 0.419 |
| Pars orbitalis | 3.11 | 0.30 | 3.06 | 0.24 | 1.266 | 0.262 |
| Pars triangularis | 3.89 | 0.35 | 3.85 | 0.30 | 0.548 | 0.460 |
| Pericalcarine cortex | 3.12 | 0.17 | 3.09 | 0.21 | 0.000 | 1.000 |
| Postcentral gyrus | 3.50 | 0.21 | 3.51 | 0.21 | 0.008 | 0.929 |
| Posterior cingulate cortex | 2.26 | 0.13 | 2.25 | 0.15 | 0.007 | 0.935 |
| Precentral gyrus | 3.43 | 0.20 | 3.44 | 0.20 | 0.022 | 0.883 |
| Precuneus | 3.12 | 0.16 | 3.12 | 0.21 | 0.637 | 0.426 |
| Rostral anterior cingulate cortex | 2.11 | 0.12 | 2.10 | 0.11 | 0.042 | 0.838 |
| Rostral middle frontal gyrus | 2.78 | 0.17 | 2.80 | 0.17 | 0.251 | 0.617 |
| Superior frontal gyrus | 2.25 | 0.10 | 2.25 | 0.10 | 0.002 | 0.963 |
| Superior parietal cortex | 3.09 | 0.13 | 3.05 | 0.16 | 2.103 | 0.148 |
| Superior temporal cortex | 4.21 | 0.33 | 4.20 | 0.29 | 0.011 | 0.916 |
| Supramarginal gyrus | 3.63 | 0.23 | 3.64 | 0.22 | 0.158 | 0.692 |
| Frontal pole | 2.12 | 0.17 | 2.16 | 0.11 | 2.025 | 0.156 |
| Temporal pole | 2.47 | 0.09 | 2.48 | 0.15 | 0.158 | 0.691 |
| Transverse temporal cortex | 4.88 | 0.43 | 4.85 | 0.38 | 0.005 | 0.941 |
| Insula | 4.44 | 0.32 | 4.36 | 0.33 | 0.707 | 0.401 |

F and P values were obtained using one-way analysis of covariance (ANCOVA) with age, sex, years of education, illness duration, and medication as covariates.

Bonferroni correction was applied; P < 0.05/66 = 0.000758.

Significant group differences are presented in a bold face.

R-MDD, remitted major depressive disorder; NR, MDD, non-remitted major depressive disorder; SD, standard deviation.

**Table S7. Comparison of the local gyrification index between drug-naïve and medicated patients with MDD**

|  |  |  |  |
| --- | --- | --- | --- |
| **Cortical regions** | **DN-MDD (n = 53)** | **M-MDD (n = 181)** | **DN-MDD vs. M-MDD** |
| **Mean** | **SD** | **Mean** | **SD** | **F (1, 227)** | **P-value** |
| ***Left hemisphere*** |  |  |  |  |  |  |
| Caudal anterior cingulate cortex | 1.88 | 0.10 | 1.91 | 0.11 | 0.742 | 0.390 |
| Caudal middle frontal gyrus | 3.12 | 0.24 | 3.21 | 0.20 | 4.007 | 0.046 |
| Cuneus | 3.02 | 0.22 | 3.07 | 0.20 | 0.146 | 0.703 |
| Entorhinal cortex | 2.61 | 0.11 | 2.64 | 0.13 | 0.810 | 0.369 |
| Fusiform gyrus | 2.76 | 0.11 | 2.78 | 0.12 | 0.003 | 0.960 |
| Inferior parietal cortex | 3.29 | 0.23 | 3.38 | 0.18 | 3.853 | 0.051 |
| Inferior temporal gyrus | 2.80 | 0.13 | 2.83 | 0.12 | 0.528 | 0.468 |
| Isthmus of cingulate cortex | 2.78 | 0.21 | 2.85 | 0.18 | 1.877 | 0.172 |
| Lateral occipital cortex | 2.69 | 0.14 | 2.72 | 0.13 | 0.024 | 0.876 |
| Lateral orbitofrontal cortex | 2.69 | 0.15 | 2.71 | 0.14 | 0.223 | 0.637 |
| Lingual gyrus | 2.85 | 0.17 | 2.87 | 0.16 | 0.336 | 0.562 |
| Medial orbitofrontal cortex | 2.14 | 0.07 | 2.16 | 0.10 | 0.677 | 0.411 |
| Middle temporal gyrus | 3.44 | 0.23 | 3.51 | 0.22 | 0.973 | 0.325 |
| Parahippocampal gyrus | 2.85 | 0.21 | 2.88 | 0.17 | 0.000 | 0.994 |
| Paracentral lobule | 2.39 | 0.23 | 2.39 | 0.11 | 0.332 | 0.565 |
| Pars opercularis | 4.18 | 0.39 | 4.27 | 0.32 | 0.824 | 0.365 |
| Pars orbitalis | 3.06 | 0.21 | 3.09 | 0.22 | 0.045 | 0.832 |
| Pars triangularis | 3.76 | 0.37 | 3.85 | 0.28 | 0.872 | 0.351 |
| Pericalcarine cortex | 2.91 | 0.18 | 2.93 | 0.19 | 0.405 | 0.525 |
| Postcentral gyrus | 3.46 | 0.31 | 3.59 | 0.20 | 8.381 | 0.004 |
| Posterior cingulate cortex | 2.23 | 0.14 | 2.26 | 0.14 | 0.511 | 0.475 |
| Precentral gyrus | 3.40 | 0.32 | 3.50 | 0.19 | 4.697 | 0.031 |
| Precuneus | 2.93 | 0.21 | 2.99 | 0.18 | 0.948 | 0.331 |
| Rostral anterior cingulate cortex | 2.04 | 0.11 | 2.07 | 0.11 | 0.702 | 0.403 |
| Rostral middle frontal gyrus | 2.75 | 0.19 | 2.82 | 0.17 | 3.397 | 0.067 |
| Superior frontal gyrus | 2.16 | 0.12 | 2.21 | 0.10 | 5.126 | 0.025 |
| Superior parietal cortex | 3.06 | 0.16 | 3.09 | 0.15 | 0.040 | 0.841 |
| Superior temporal cortex | 4.13 | 0.32 | 4.26 | 0.29 | 3.396 | 0.067 |
| Supramarginal gyrus | 3.54 | 0.30 | 3.68 | 0.20 | 11.002 | 0.001 |
| Frontal pole | 2.11 | 0.13 | 2.12 | 0.11 | 0.136 | 0.713 |
| Temporal pole | 2.51 | 0.27 | 2.50 | 0.15 | 0.195 | 0.659 |
| Transverse temporal cortex | 4.72 | 0.39 | 4.88 | 0.37 | 3.615 | 0.059 |
| Insula | 4.28 | 0.44 | 4.42 | 0.32 | 3.756 | 0.054 |
| *Right hemisphere* |  |  |  |  |  |  |
| Caudal anterior cingulate cortex | 1.94 | 0.12 | 1.97 | 0.11 | 0.719 | 0.397 |
| Caudal middle frontal gyrus | 3.10 | 0.19 | 3.18 | 0.19 | 3.724 | 0.055 |
| Cuneus | 3.20 | 0.21 | 3.26 | 0.21 | 0.914 | 0.340 |
| Entorhinal cortex | 2.65 | 0.11 | 2.65 | 0.14 | 1.110 | 0.293 |
| Fusiform gyrus | 2.74 | 0.11 | 2.75 | 0.13 | 0.462 | 0.497 |
| Inferior parietal cortex | 3.29 | 0.18 | 3.37 | 0.18 | 2.461 | 0.118 |
| Inferior temporal gyrus | 2.73 | 0.11 | 2.76 | 0.13 | 0.025 | 0.876 |
| Isthmus of cingulate cortex | 2.91 | 0.22 | 2.94 | 0.20 | 0.007 | 0.934 |
| Lateral occipital cortex | 2.71 | 0.11 | 2.75 | 0.13 | 0.482 | 0.488 |
| Lateral orbitofrontal cortex | 2.59 | 0.15 | 2.66 | 0.14 | 4.140 | 0.043 |
| Lingual gyrus | 2.95 | 0.19 | 2.97 | 0.18 | 0.428 | 0.514 |
| Medial orbitofrontal cortex | 2.14 | 0.08 | 2.17 | 0.11 | 0.238 | 0.626 |
| Middle temporal gyrus | 3.38 | 0.19 | 3.44 | 0.22 | 0.427 | 0.514 |
| Parahippocampal gyrus | 2.90 | 0.16 | 2.89 | 0.18 | 3.473 | 0.064 |
| Paracentral lobule | 2.36 | 0.14 | 2.40 | 0.13 | 1.850 | 0.175 |
| Pars opercularis | 4.20 | 0.33 | 4.30 | 0.35 | 1.069 | 0.302 |
| Pars orbitalis | 2.99 | 0.24 | 3.09 | 0.24 | 4.370 | 0.038 |
| Pars triangularis | 3.78 | 0.35 | 3.88 | 0.29 | 1.523 | 0.219 |
| Pericalcarine cortex | 3.05 | 0.20 | 3.10 | 0.21 | 0.399 | 0.528 |
| Postcentral gyrus | 3.43 | 0.20 | 3.54 | 0.21 | 6.305 | 0.013 |
| Posterior cingulate cortex | 2.23 | 0.15 | 2.26 | 0.14 | 0.793 | 0.374 |
| Precentral gyrus | 3.38 | 0.20 | 3.46 | 0.20 | 3.653 | 0.057 |
| Precuneus | 3.07 | 0.21 | 3.14 | 0.21 | 1.030 | 0.311 |
| Rostral anterior cingulate cortex | 2.08 | 0.10 | 2.11 | 0.12 | 0.907 | 0.342 |
| Rostral middle frontal gyrus | 2.74 | 0.17 | 2.81 | 0.17 | 4.202 | 0.042 |
| Superior frontal gyrus | 2.20 | 0.10 | 2.26 | 0.10 | 9.911 | 0.002 |
| Superior parietal cortex | 3.00 | 0.16 | 3.07 | 0.15 | 4.552 | 0.034 |
| Superior temporal cortex | 4.12 | 0.29 | 4.23 | 0.29 | 2.175 | 0.142 |
| Supramarginal gyrus | 3.55 | 0.21 | 3.67 | 0.22 | 6.795 | 0.010 |
| Frontal pole | 2.13 | 0.10 | 2.16 | 0.12 | 1.857 | 0.174 |
| Temporal pole | 2.44 | 0.13 | 2.49 | 0.15 | 1.102 | 0.295 |
| Transverse temporal cortex | 4.73 | 0.35 | 4.89 | 0.39 | 3.123 | 0.079 |
| Insula | 4.30 | 0.31 | 4.39 | 0.33 | 0.258 | 0.612 |

F and P values were obtained using one-way analysis of covariance (ANCOVA) with age, sex, years of education, HDRS score, and illness duration as covariates.

Bonferroni correction was applied; P < 0.05/66 = 0.000758.

Significant group differences are presented in a bold face.

DN-MDD, drug-naïve patients with major depressive disorder; M-MDD, medicated patients with major depressive disorder; SD, standard deviation.

**Table S8. Correlation analysis between local gyrification index and fluoxetine-equivalent dose in patients with major depressive disorder**

|  |  |
| --- | --- |
| **Cortical regions** | **Fluoxetine-equivalent dose** |
| **r** | **P** |
| ***Left hemisphere*** |  |  |
| Caudal anterior cingulate cortex | 0.013 | 0.848  |
| Caudal middle frontal gyrus | 0.103 | 0.120  |
| Cuneus | 0.057 | 0.390  |
| Entorhinal cortex | 0.096 | 0.146  |
| Fusiform gyrus | 0.077 | 0.243  |
| Inferior parietal cortex | 0.082 | 0.215  |
| Inferior temporal gyrus | 0.089 | 0.182  |
| Isthmus of cingulate cortex | 0.040 | 0.551  |
| Lateral occipital cortex | 0.045 | 0.494  |
| Lateral orbitofrontal cortex | 0.053 | 0.429  |
| Lingual gyrus | -0.032 | 0.629  |
| Medial orbitofrontal cortex | 0.092 | 0.166  |
| Middle temporal gyrus | 0.067 | 0.314  |
| Parahippocampal gyrus | 0.010 | 0.874  |
| Paracentral lobule | -0.023 | 0.725  |
| Pars opercularis | 0.078 | 0.239  |
| Pars orbitalis | 0.046 | 0.488  |
| Pars triangularis | 0.042 | 0.532  |
| Pericalcarine cortex | -0.005 | 0.936  |
| Postcentral gyrus | 0.121 | 0.068  |
| Posterior cingulate cortex | 0.046 | 0.485  |
| Precentral gyrus | 0.096 | 0.146  |
| Precuneus | 0.088 | 0.184  |
| Rostral anterior cingulate cortex | 0.062 | 0.348  |
| Rostral middle frontal gyrus | 0.120 | 0.071  |
| Superior frontal gyrus | 0.078 | 0.241  |
| Superior parietal cortex | 0.009 | 0.888  |
| Superior temporal cortex | 0.104 | 0.117  |
| Supramarginal gyrus | 0.117 | 0.078  |
| Frontal pole | 0.076 | 0.250  |
| Temporal pole | 0.013 | 0.840  |
| Transverse temporal cortex | 0.070 | 0.290  |
| Insula | 0.092 | 0.166  |
| ***Right hemisphere*** |  |  |
| Caudal anterior cingulate cortex | 0.026 | 0.699  |
| Caudal middle frontal gyrus | 0.130 | 0.049  |
| Cuneus | 0.058 | 0.381  |
| Entorhinal cortex | 0.026 | 0.697  |
| Fusiform gyrus | 0.063 | 0.341  |
| Inferior parietal cortex | 0.100 | 0.130  |
| Inferior temporal gyrus | 0.135 | 0.041  |
| Isthmus of cingulate cortex | -0.002 | 0.977  |
| Lateral occipital cortex | 0.113 | 0.089  |
| Lateral orbitofrontal cortex | 0.123 | 0.064  |
| Lingual gyrus | -0.015 | 0.822  |
| Medial orbitofrontal cortex | 0.080 | 0.226  |
| Middle temporal gyrus | 0.098 | 0.140  |
| Parahippocampal gyrus | -0.034 | 0.608  |
| Paracentral lobule | 0.050 | 0.452  |
| Pars opercularis | 0.030 | 0.654  |
| Pars orbitalis | 0.134 | 0.043  |
| Pars triangularis | 0.076 | 0.253  |
| Pericalcarine cortex | 0.050 | 0.453  |
| Postcentral gyrus | 0.155 | 0.019  |
| Posterior cingulate cortex | 0.024 | 0.722  |
| Precentral gyrus | 0.119 | 0.072  |
| Precuneus | 0.068 | 0.305  |
| Rostral anterior cingulate cortex | 0.034 | 0.609  |
| Rostral middle frontal gyrus | 0.060 | 0.365  |
| Superior frontal gyrus | 0.137 | 0.038  |
| Superior parietal cortex | 0.075 | 0.256  |
| Superior temporal cortex | 0.133 | 0.045  |
| Supramarginal gyrus | 0.124 | 0.061  |
| Frontal pole | 0.080 | 0.227  |
| Temporal pole | 0.101 | 0.127  |
| Transverse temporal cortex | 0.141 | 0.033  |
| Insula | 0.088 | 0.185  |

A two-tailed Pearson's partial correlation analysis was performed, controlling for age, sex, years of education, illness duration, and HDRS score as covariates.

Bonferroni correction was applied: P < 0.05/66 = 0.000758

Significant correlations were presented in a bold face.

**Table S9. Correlation analysis between local gyrification index and olanzapine-equivalent dose in patients with major depressive disorder**

|  |  |
| --- | --- |
| **Cortical regions** | **Olanzapine-equivalent dose** |
| **r** | **P** |
| ***Left hemisphere*** |  |  |
| Caudal anterior cingulate cortex | -0.071 | 0.285  |
| Caudal middle frontal gyrus | -0.093 | 0.160  |
| Cuneus | -0.061 | 0.362  |
| Entorhinal cortex | -0.070 | 0.290  |
| Fusiform gyrus | -0.099 | 0.133  |
| Inferior parietal cortex | -0.024 | 0.718  |
| Inferior temporal gyrus | -0.100 | 0.130  |
| Isthmus of cingulate cortex | -0.172 | 0.009  |
| Lateral occipital cortex | -0.085 | 0.200  |
| Lateral orbitofrontal cortex | -0.083 | 0.211  |
| Lingual gyrus | -0.125 | 0.060  |
| Medial orbitofrontal cortex | -0.011 | 0.865  |
| Middle temporal gyrus | -0.079 | 0.235  |
| Parahippocampal gyrus | -0.062 | 0.348  |
| Paracentral lobule | -0.095 | 0.154  |
| Pars opercularis | -0.171 | 0.010  |
| Pars orbitalis | -0.072 | 0.277  |
| Pars triangularis | -0.119 | 0.072  |
| Pericalcarine cortex | -0.107 | 0.105  |
| Postcentral gyrus | -0.055 | 0.410  |
| Posterior cingulate cortex | -0.160 | 0.015  |
| Precentral gyrus | -0.080 | 0.230  |
| Precuneus | -0.106 | 0.110  |
| Rostral anterior cingulate cortex | -0.017 | 0.797  |
| Rostral middle frontal gyrus | -0.072 | 0.276  |
| Superior frontal gyrus | -0.090 | 0.174  |
| Superior parietal cortex | -0.058 | 0.381  |
| Superior temporal cortex | -0.073 | 0.268  |
| Supramarginal gyrus | -0.054 | 0.414  |
| Frontal pole | 0.077 | 0.243  |
| Temporal pole | -0.029 | 0.665  |
| Transverse temporal cortex | -0.088 | 0.185  |
| Insula | -0.088 | 0.186  |
| ***Right hemisphere*** |  |  |
| Caudal anterior cingulate cortex | -0.085 | 0.202  |
| Caudal middle frontal gyrus | -0.025 | 0.704  |
| Cuneus | -0.110 | 0.096  |
| Entorhinal cortex | -0.106 | 0.110  |
| Fusiform gyrus | -0.141 | 0.033  |
| Inferior parietal cortex | -0.052 | 0.437  |
| Inferior temporal gyrus | -0.038 | 0.567  |
| Isthmus of cingulate cortex | -0.200 | 0.002  |
| Lateral occipital cortex | -0.107 | 0.107  |
| Lateral orbitofrontal cortex | -0.029 | 0.667  |
| Lingual gyrus | -0.168 | 0.011  |
| Medial orbitofrontal cortex | -0.028 | 0.676  |
| Middle temporal gyrus | -0.046 | 0.490  |
| Parahippocampal gyrus | -0.150 | 0.023  |
| Paracentral lobule | -0.052 | 0.436  |
| Pars opercularis | -0.035 | 0.601  |
| Pars orbitalis | -0.090 | 0.175  |
| Pars triangularis | -0.041 | 0.538  |
| Pericalcarine cortex | -0.117 | 0.078  |
| Postcentral gyrus | -0.042 | 0.525  |
| Posterior cingulate cortex | -0.110 | 0.098  |
| Precentral gyrus | -0.061 | 0.360  |
| Precuneus | -0.108 | 0.102  |
| Rostral anterior cingulate cortex | -0.068 | 0.304  |
| Rostral middle frontal gyrus | -0.035 | 0.596  |
| Superior frontal gyrus | -0.039 | 0.557  |
| Superior parietal cortex | -0.052 | 0.436  |
| Superior temporal cortex | -0.031 | 0.645  |
| Supramarginal gyrus | 0.003 | 0.964  |
| Frontal pole | 0.027 | 0.688  |
| Temporal pole | -0.070 | 0.295  |
| Transverse temporal cortex | -0.009 | 0.893  |
| Insula | -0.033 | 0.618  |

A two-tailed Pearson's partial correlation analysis was performed, controlling for age, sex, years of education, illness duration, and HDRS score as covariates.

Bonferroni correction was applied: P < 0.05/66 = 0.000758

**Table S10. Correlation analysis between the local gyrification index, illness duration, and depression severity in patients with major depressive disorder**

|  |  |  |
| --- | --- | --- |
| **Cortical regions** | **Illness duration** | **HDRS** |
| **r** | **P** | **r** | **P** |
| ***Left hemisphere*** |  |  |  |  |
| Caudal anterior cingulate cortex | -0.007 | 0.920 | 0.001 | 0.986 |
| Caudal middle frontal gyrus | -0.043 | 0.513 | 0.087 | 0.192 |
| Cuneus | 0.194 | 0.003 | 0.013 | 0.841 |
| Entorhinal cortex | 0.122 | 0.066 | 0.040 | 0.548 |
| Fusiform gyrus | 0.200 | 0.002 | 0.094 | 0.157 |
| Inferior parietal cortex | 0.175 | 0.008 | 0.035 | 0.600 |
| **Inferior temporal gyrus** | **0.238** | **2.75 × 10-4** | 0.130 | 0.050 |
| Isthmus of cingulate cortex | 0.170 | 0.010 | 0.000 | 0.996 |
| **Lateral occipital cortex** | **0.285** | **1.21× 10-5** | 0.016 | 0.806 |
| Lateral orbitofrontal cortex | 0.018 | 0.788 | 0.108 | 0.103 |
| Lingual gyrus | 0.180 | 0.006 | 0.026 | 0.697 |
| Medial orbitofrontal cortex | 0.040 | 0.546 | -0.036 | 0.588 |
| Middle temporal gyrus | 0.199 | 0.003 | 0.098 | 0.138 |
| Parahippocampal gyrus | 0.090 | 0.174 | 0.022 | 0.736 |
| Paracentral lobule | -0.024 | 0.712 | -0.114 | 0.086 |
| Pars opercularis | 0.061 | 0.361 | 0.065 | 0.326 |
| Pars orbitalis | 0.057 | 0.389 | 0.013 | 0.842 |
| Pars triangularis | 0.086 | 0.195 | -0.005 | 0.946 |
| Pericalcarine cortex | 0.199 | 0.002 | 0.014 | 0.837 |
| Postcentral gyrus | 0.037 | 0.574 | 0.045 | 0.493 |
| Posterior cingulate cortex | 0.014 | 0.835 | -0.062 | 0.347 |
| Precentral gyrus | 0.060 | 0.366 | 0.043 | 0.520 |
| Precuneus | 0.180 | 0.006 | -0.015 | 0.817 |
| Rostral anterior cingulate cortex | -0.008 | 0.902 | -0.031 | 0.643 |
| Rostral middle frontal gyrus | 0.146 | 0.027 | 0.040 | 0.543 |
| Superior frontal gyrus | -0.049 | 0.460 | 0.054 | 0.416 |
| Superior parietal cortex | 0.086 | 0.197 | -0.008 | 0.906 |
| Superior temporal cortex | 0.105 | 0.113 | 0.098 | 0.141 |
| Supramarginal gyrus | 0.087 | 0.187 | 0.096 | 0.147 |
| Frontal pole | -0.013 | 0.840 | 0.056 | 0.403 |
| Temporal pole | 0.020 | 0.769 | 0.054 | 0.416 |
| Transverse temporal cortex | 0.087 | 0.189 | 0.098 | 0.140 |
| Insula | 0.070 | 0.289 | 0.132 | 0.046 |
| *Right hemisphere* |  |  |  |  |
| Caudal anterior cingulate cortex | 0.008 | 0.904 | -0.016 | 0.812 |
| Caudal middle frontal gyrus | -0.041 | 0.537 | 0.030 | 0.651 |
| Cuneus | 0.193 | 0.003 | 0.001 | 0.993 |
| Entorhinal cortex | 0.182 | 0.006 | -0.062 | 0.351 |
| Fusiform gyrus | 0.195 | 0.003 | -0.031 | 0.637 |
| Inferior parietal cortex | 0.188 | 0.004 | 0.017 | 0.800 |
| Inferior temporal gyrus | 0.220 | 0.001 | -0.051 | 0.439 |
| Isthmus of cingulate cortex | 0.137 | 0.038 | 0.017 | 0.804 |
| **Lateral occipital cortex** | **0.333** | **2.49 × 10-7** | -0.103 | 0.121 |
| Lateral orbitofrontal cortex | 0.058 | 0.381 | 0.046 | 0.486 |
| Lingual gyrus | 0.211 | 0.001 | -0.041 | 0.534 |
| Medial orbitofrontal cortex | 0.150 | 0.023 | -0.043 | 0.517 |
| Middle temporal gyrus | 0.099 | 0.136 | 0.010 | 0.874 |
| Parahippocampal gyrus | 0.131 | 0.047 | -0.103 | 0.120 |
| Paracentral lobule | -0.030 | 0.649 | -0.025 | 0.702 |
| Pars opercularis | 0.037 | 0.576 | -0.017 | 0.801 |
| Pars orbitalis | 0.014 | 0.831 | 0.014 | 0.837 |
| Pars triangularis | -0.002 | 0.974 | -0.043 | 0.517 |
| Pericalcarine cortex | 0.209 | 0.001 | -0.004 | 0.946 |
| Postcentral gyrus | -0.005 | 0.938 | 0.043 | 0.517 |
| Posterior cingulate cortex | 0.006 | 0.933 | -0.008 | 0.900 |
| Precentral gyrus | 0.041 | 0.535 | 0.037 | 0.582 |
| Precuneus | 0.141 | 0.033 | 0.028 | 0.672 |
| Rostral anterior cingulate cortex | 0.086 | 0.197 | -0.048 | 0.474 |
| Rostral middle frontal gyrus | 0.009 | 0.889 | 0.050 | 0.454 |
| Superior frontal gyrus | -0.091 | 0.170 | 0.096 | 0.146 |
| Superior parietal cortex | 0.113 | 0.088 | -0.019 | 0.771 |
| Superior temporal cortex | 0.064 | 0.337 | 0.055 | 0.407 |
| Supramarginal gyrus | 0.068 | 0.305 | 0.061 | 0.359 |
| Frontal pole | -0.038 | 0.572 | 0.076 | 0.249 |
| Temporal pole | 0.145 | 0.028 | -0.040 | 0.544 |
| Transverse temporal cortex | 0.087 | 0.189 | 0.048 | 0.469 |
| Insula | 0.103 | 0.119 | -0.055 | 0.405 |

A two-tailed Pearson's partial correlation analysis was performed, controlling for age, sex, years of education, illness duration (for HDRS score analysis), HDRS score (for illness duration analysis), and medication as covariates.

Bonferroni correction was applied; P < 0.05/66 = 0.000758.

Significant correlations are presented in a bold face.

HDRS, Hamilton Depression Rating Scale score.