

## Supplementary Material

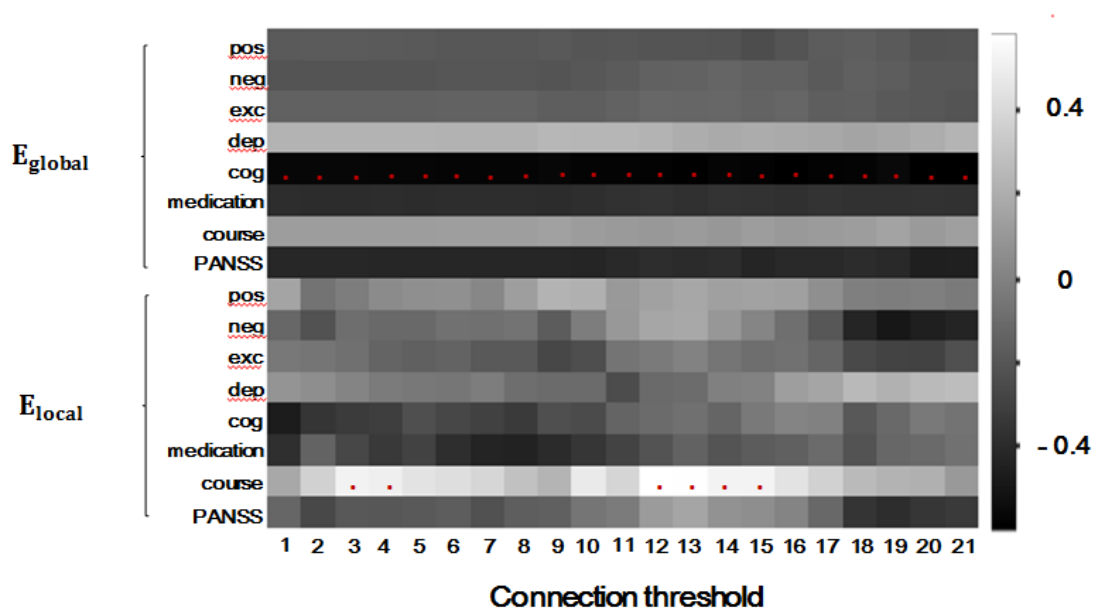


Figure S1. Relationship between topological properties (global efficiency  $E_{global}$ , and local efficiency  $E_{local}$ ) and clinical variables [course of illness, medication doses, total scores of PANSS (PANSS\_T) and 5-factor model of schizophrenic psychopathology: positive (pos), delusion and grandiosity; negative (neg), emotional withdrawal, poor rapport, and social withdrawal; excitement (exc), excitement and hostility; cognition (cog), conceptual disorganization and abstract thinking; depression and anxiety (dep), anxiety, guilt feeling, and depression<sup>[1, 2]</sup>.] at each of connection threshold in patients with schizophrenia. Partial correlation coefficient was used to assess the significance of a partial correlation between topological properties and clinical variables controlled for three potentially confounding variables (age, gender and brain size). The coefficient value for each pair of variables is indicated with a colored bar. The dotted red square means that a partial correlation is statistically significant at the  $p < 0.05$  level (uncorrected).

**Table S1. Comparisons of network global efficiency between schizophrenic patients (SZ) and young normal controls (NC1)**

| Threshold | Mean $\pm$ SD      |                    | F-value | <i>p</i> -value* |
|-----------|--------------------|--------------------|---------|------------------|
|           | SZ (n=19)          | NC1 (n=24)         |         |                  |
| 1         | 26.569 $\pm$ 0.355 | 27.646 $\pm$ 0.315 | 5.048   | 0.031            |
| 2         | 26.568 $\pm$ 0.355 | 27.646 $\pm$ 0.315 | 5.058   | 0.030            |
| 3         | 26.567 $\pm$ 0.355 | 27.643 $\pm$ 0.315 | 5.016   | 0.031            |
| 4         | 26.564 $\pm$ 0.355 | 27.641 $\pm$ 0.315 | 5.036   | 0.031            |
| 5         | 26.561 $\pm$ 0.355 | 27.634 $\pm$ 0.315 | 4.989   | 0.031            |
| 6         | 26.541 $\pm$ 0.356 | 27.628 $\pm$ 0.316 | 5.098   | 0.030            |
| 7         | 26.543 $\pm$ 0.355 | 27.612 $\pm$ 0.315 | 4.977   | 0.032            |
| 8         | 26.541 $\pm$ 0.354 | 27.572 $\pm$ 0.314 | 4.627   | 0.038            |
| 9         | 26.500 $\pm$ 0.358 | 27.545 $\pm$ 0.317 | 4.676   | 0.037            |
| 10        | 26.453 $\pm$ 0.355 | 27.524 $\pm$ 0.315 | 4.981   | 0.032            |
| 11        | 26.374 $\pm$ 0.355 | 27.483 $\pm$ 0.315 | 5.335   | 0.026            |
| 12        | 26.328 $\pm$ 0.353 | 27.420 $\pm$ 0.313 | 5.235   | 0.028            |
| 13        | 26.244 $\pm$ 0.359 | 27.364 $\pm$ 0.318 | 5.345   | 0.026            |
| 14        | 26.183 $\pm$ 0.354 | 27.311 $\pm$ 0.314 | 5.557   | 0.024            |
| 15        | 26.096 $\pm$ 0.356 | 27.253 $\pm$ 0.316 | 5.777   | 0.021            |
| 16        | 26.023 $\pm$ 0.357 | 27.204 $\pm$ 0.316 | 6.011   | 0.019            |
| 17        | 25.937 $\pm$ 0.354 | 27.156 $\pm$ 0.315 | 6.479   | 0.015            |
| 18        | 25.789 $\pm$ 0.362 | 27.059 $\pm$ 0.321 | 6.752   | 0.013            |
| 19        | 25.678 $\pm$ 0.370 | 26.915 $\pm$ 0.329 | 6.114   | 0.018            |
| 20        | 25.556 $\pm$ 0.370 | 26.853 $\pm$ 0.328 | 6.724   | 0.013            |
| 21        | 25.479 $\pm$ 0.374 | 26.752 $\pm$ 0.332 | 6.331   | 0.016            |

\* *p*-values were calculated using a general linear model after adjusting for the effects of gender, age and brain size.

**Table S2. Comparisons of network local efficiency between schizophrenic patients (SZ) and young normal controls (NC1)**

| Threshold | Mean $\pm$ SD      |                    | F-value | $p$ -value* |
|-----------|--------------------|--------------------|---------|-------------|
|           | SZ (n=19)          | NC1 (n=24)         |         |             |
| 1         | 38.368 $\pm$ 0.335 | 40.596 $\pm$ 0.475 | 9.494   | 0.004       |
| 2         | 40.146 $\pm$ 0.609 | 41.909 $\pm$ 0.540 | 4.589   | 0.039       |
| 3         | 41.391 $\pm$ 0.627 | 43.101 $\pm$ 0.557 | 4.066   | 0.051       |
| 4         | 42.108 $\pm$ 0.748 | 44.024 $\pm$ 0.664 | 3.589   | 0.066       |
| 5         | 42.566 $\pm$ 0.728 | 44.424 $\pm$ 0.646 | 3.564   | 0.067       |
| 6         | 43.061 $\pm$ 0.687 | 44.865 $\pm$ 0.610 | 3.771   | 0.060       |
| 7         | 44.342 $\pm$ 0.701 | 45.493 $\pm$ 0.622 | 5.151   | 0.029       |
| 8         | 43.902 $\pm$ 0.755 | 45.867 $\pm$ 0.670 | 3.705   | 0.062       |
| 9         | 44.035 $\pm$ 0.716 | 46.371 $\pm$ 0.636 | 5.825   | 0.021       |
| 10        | 44.704 $\pm$ 0.766 | 46.612 $\pm$ 0.679 | 3.399   | 0.073       |
| 11        | 44.978 $\pm$ 0.723 | 46.610 $\pm$ 0.641 | 2.794   | 0.103       |
| 12        | 44.602 $\pm$ 0.695 | 46.675 $\pm$ 0.617 | 4.876   | 0.033       |
| 13        | 44.584 $\pm$ 0.752 | 46.953 $\pm$ 0.667 | 5.435   | 0.025       |
| 14        | 44.975 $\pm$ 0.837 | 47.265 $\pm$ 0.742 | 4.101   | 0.050       |
| 15        | 45.006 $\pm$ 0.853 | 47.202 $\pm$ 0.757 | 3.629   | 0.064       |
| 16        | 44.876 $\pm$ 0.812 | 46.854 $\pm$ 0.721 | 3.245   | 0.080       |
| 17        | 44.820 $\pm$ 0.866 | 46.744 $\pm$ 0.768 | 2.702   | 0.108       |
| 18        | 43.632 $\pm$ 0.870 | 46.601 $\pm$ 0.772 | 6.374   | 0.016       |
| 19        | 43.648 $\pm$ 0.927 | 46.565 $\pm$ 0.823 | 5.422   | 0.025       |
| 20        | 43.420 $\pm$ 0.946 | 46.740 $\pm$ 0.839 | 6.742   | 0.013       |
| 21        | 43.447 $\pm$ 1.014 | 46.610 $\pm$ 0.900 | 5.327   | 0.027       |

\*  $p$ -values were calculated using a general linear model after adjusting for the effects of gender, age and brain size.

**Table S3. Comparisons of network global efficiency between unaffected parents of schizophrenic patients (PA) and old normal controls (NC2)**

| Threshold | Mean $\pm$ SD      |                    | F-value | $p$ -value* |
|-----------|--------------------|--------------------|---------|-------------|
|           | PA (n=41)          | NC2 (n=26)         |         |             |
| 1         | 26.103 $\pm$ 0.240 | 26.465 $\pm$ 0.303 | 0.862   | 0.357       |
| 2         | 26.103 $\pm$ 0.240 | 26.464 $\pm$ 0.303 | 0.855   | 0.359       |
| 3         | 26.102 $\pm$ 0.240 | 26.462 $\pm$ 0.303 | 0.851   | 0.360       |
| 4         | 26.094 $\pm$ 0.240 | 26.458 $\pm$ 0.302 | 0.876   | 0.353       |
| 5         | 26.081 $\pm$ 0.240 | 26.455 $\pm$ 0.302 | 0.925   | 0.340       |
| 6         | 26.066 $\pm$ 0.241 | 26.439 $\pm$ 0.304 | 0.908   | 0.344       |
| 7         | 26.047 $\pm$ 0.243 | 26.417 $\pm$ 0.306 | 0.882   | 0.351       |
| 8         | 26.016 $\pm$ 0.244 | 26.394 $\pm$ 0.308 | 0.907   | 0.345       |
| 9         | 25.967 $\pm$ 0.248 | 26.347 $\pm$ 0.313 | 0.889   | 0.349       |
| 10        | 25.926 $\pm$ 0.250 | 26.323 $\pm$ 0.315 | 0.958   | 0.331       |
| 11        | 25.868 $\pm$ 0.255 | 26.259 $\pm$ 0.321 | 0.893   | 0.348       |
| 12        | 25.806 $\pm$ 0.257 | 26.199 $\pm$ 0.324 | 0.890   | 0.349       |
| 13        | 25.743 $\pm$ 0.254 | 26.156 $\pm$ 0.321 | 0.997   | 0.322       |
| 14        | 25.681 $\pm$ 0.257 | 26.114 $\pm$ 0.324 | 1.074   | 0.304       |
| 15        | 25.608 $\pm$ 0.257 | 26.036 $\pm$ 0.325 | 1.044   | 0.311       |
| 16        | 25.547 $\pm$ 0.257 | 25.968 $\pm$ 0.324 | 1.013   | 0.318       |
| 17        | 25.474 $\pm$ 0.261 | 25.886 $\pm$ 0.329 | 0.943   | 0.335       |
| 18        | 25.402 $\pm$ 0.262 | 25.837 $\pm$ 0.330 | 1.043   | 0.311       |
| 19        | 25.329 $\pm$ 0.264 | 25.744 $\pm$ 0.332 | 0.939   | 0.336       |
| 20        | 25.227 $\pm$ 0.267 | 25.609 $\pm$ 0.337 | 0.771   | 0.383       |
| 21        | 25.118 $\pm$ 0.268 | 25.542 $\pm$ 0.338 | 0.951   | 0.333       |

\*  $p$ -values were calculated using a general linear model after adjusting for the effects of gender, age and brain size.

**Table S4. Comparisons of network local efficiency between unaffected parents of schizophrenic patients (PA) and old normal controls (NC2)**

| Threshold | Mean $\pm$ SD      |                    | F-value | <i>p</i> -value* |
|-----------|--------------------|--------------------|---------|------------------|
|           | PA (n=41)          | NC2 (n=26)         |         |                  |
| 1         | 38.138 $\pm$ 0.384 | 37.928 $\pm$ 0.484 | 0.113   | 0.738            |
| 2         | 40.050 $\pm$ 0.428 | 39.909 $\pm$ 0.540 | 0.041   | 0.841            |
| 3         | 40.913 $\pm$ 0.482 | 40.970 $\pm$ 0.608 | 0.005   | 0.943            |
| 4         | 41.381 $\pm$ 0.503 | 41.898 $\pm$ 0.635 | 0.007   | 0.935            |
| 5         | 42.077 $\pm$ 0.497 | 42.523 $\pm$ 0.627 | 0.305   | 0.583            |
| 6         | 42.587 $\pm$ 0.522 | 42.747 $\pm$ 0.658 | 0.036   | 0.851            |
| 7         | 42.989 $\pm$ 0.520 | 43.121 $\pm$ 0.656 | 0.024   | 0.877            |
| 8         | 43.390 $\pm$ 0.488 | 43.218 $\pm$ 0.615 | 0.047   | 0.829            |
| 9         | 43.862 $\pm$ 0.482 | 43.447 $\pm$ 0.608 | 0.281   | 0.598            |
| 10        | 43.971 $\pm$ 0.466 | 43.703 $\pm$ 0.588 | 0.125   | 0.725            |
| 11        | 44.109 $\pm$ 0.503 | 43.838 $\pm$ 0.635 | 0.110   | 0.741            |
| 12        | 44.026 $\pm$ 0.497 | 44.026 $\pm$ 0.627 | <0.001  | 0.999            |
| 13        | 44.294 $\pm$ 0.519 | 43.878 $\pm$ 0.654 | 0.245   | 0.623            |
| 14        | 44.338 $\pm$ 0.515 | 44.042 $\pm$ 0.649 | 0.125   | 0.725            |
| 15        | 44.203 $\pm$ 0.518 | 43.978 $\pm$ 0.654 | 0.072   | 0.789            |
| 16        | 44.207 $\pm$ 0.552 | 43.666 $\pm$ 0.696 | 0.363   | 0.549            |
| 17        | 43.856 $\pm$ 0.597 | 43.747 $\pm$ 0.753 | 0.013   | 0.911            |
| 18        | 43.582 $\pm$ 0.611 | 43.872 $\pm$ 0.771 | <0.001  | 0.984            |
| 19        | 43.655 $\pm$ 0.649 | 43.921 $\pm$ 0.819 | 0.063   | 0.802            |
| 20        | 43.551 $\pm$ 0.668 | 43.506 $\pm$ 0.843 | 0.002   | 0.967            |
| 21        | 43.344 $\pm$ 0.673 | 43.404 $\pm$ 0.848 | 0.003   | 0.957            |

\* *p*-values were calculated using a general linear model after adjusting for the effects of gender, age and brain size.

**Table S5. Comparisons of overall connectivity strength between schizophrenic patients (SZ) and young normal controls (NC1)**

| Threshold | Mean Value $\pm$ SD |                  | F-value | <i>p</i> -value* |
|-----------|---------------------|------------------|---------|------------------|
|           | SZ (n=19)           | NC1 (n=24)       |         |                  |
| 1         | 888.2 $\pm$ 63.9    | 883.6 $\pm$ 51.9 | 0.066   | 0.799            |
| 2         | 768.1 $\pm$ 53.8    | 765.7 $\pm$ 42.8 | 0.026   | 0.872            |
| 3         | 696.4 $\pm$ 48.7    | 695.9 $\pm$ 40.1 | 0.001   | 0.974            |
| 4         | 639.9 $\pm$ 45.4    | 642.8 $\pm$ 34.6 | 0.053   | 0.819            |
| 5         | 595.8 $\pm$ 43.5    | 600.5 $\pm$ 32.0 | 0.170   | 0.682            |
| 6         | 559.3 $\pm$ 42.5    | 562.8 $\pm$ 33.8 | 0.094   | 0.760            |
| 7         | 527.9 $\pm$ 40.6    | 531.0 $\pm$ 31.2 | 0.081   | 0.778            |
| 8         | 500.6 $\pm$ 40.1    | 504.9 $\pm$ 27.9 | 0.167   | 0.685            |
| 9         | 477.9 $\pm$ 38.2    | 481.2 $\pm$ 26.6 | 0.110   | 0.742            |
| 10        | 455.5 $\pm$ 38.1    | 459.0 $\pm$ 27.6 | 0.124   | 0.727            |
| 11        | 434.8 $\pm$ 35.6    | 437.9 $\pm$ 27.5 | 0.103   | 0.750            |
| 12        | 415.5 $\pm$ 36.3    | 419.3 $\pm$ 27.4 | 0.152   | 0.699            |
| 13        | 397.6 $\pm$ 34.5    | 404.7 $\pm$ 26.8 | 0.575   | 0.453            |
| 14        | 382.4 $\pm$ 33.2    | 389.8 $\pm$ 25.9 | 0.688   | 0.412            |
| 15        | 368.2 $\pm$ 31.3    | 374.0 $\pm$ 26.4 | 0.447   | 0.507            |
| 16        | 355.7 $\pm$ 30.3    | 360.5 $\pm$ 26.1 | 0.312   | 0.579            |
| 17        | 345.2 $\pm$ 30.1    | 347.5 $\pm$ 25.1 | 0.075   | 0.786            |
| 18        | 332.6 $\pm$ 30.7    | 336.3 $\pm$ 25.8 | 0.177   | 0.676            |
| 19        | 321.3 $\pm$ 30.6    | 326.1 $\pm$ 25.4 | 0.319   | 0.576            |
| 20        | 312.3 $\pm$ 30.1    | 315.7 $\pm$ 26.2 | 0.157   | 0.694            |
| 21        | 302.8 $\pm$ 30.2    | 305.8 $\pm$ 25.0 | 0.124   | 0.727            |

\* *p*-values were calculated using a general linear model after adjusting for the effects of gender, age and brain size.

**Table S6. Comparisons of overall connectivity strength between unaffected parents of schizophrenic patients (PA) and young normal controls (NC2)**

| Threshold | Mean Value $\pm$ SD |                  | F-value | <i>p</i> -value* |
|-----------|---------------------|------------------|---------|------------------|
|           | PA (n=41)           | NC2 (n=26)       |         |                  |
| 1         | 872.7 $\pm$ 66.8    | 896.7 $\pm$ 58.2 | 2.263   | 0.137            |
| 2         | 758.8 $\pm$ 54.1    | 770.6 $\pm$ 49.8 | 0.843   | 0.362            |
| 3         | 688.6 $\pm$ 48.0    | 692.7 $\pm$ 44.6 | 0.122   | 0.728            |
| 4         | 635.0 $\pm$ 42.9    | 638.3 $\pm$ 40.6 | 0.093   | 0.761            |
| 5         | 592.4 $\pm$ 40.8    | 593.2 $\pm$ 37.4 | 0.007   | 0.935            |
| 6         | 556.3 $\pm$ 39.8    | 556.6 $\pm$ 37.2 | 0.001   | 0.975            |
| 7         | 524.3 $\pm$ 38.3    | 524.3 $\pm$ 36.1 | <0.001  | 0.997            |
| 8         | 496.3 $\pm$ 36.7    | 498.2 $\pm$ 33.6 | 0.043   | 0.837            |
| 9         | 471.2 $\pm$ 35.0    | 475.1 $\pm$ 33.8 | 0.200   | 0.656            |
| 10        | 449.0 $\pm$ 34.8    | 451.5 $\pm$ 34.0 | 0.078   | 0.781            |
| 11        | 427.3 $\pm$ 34.1    | 431.6 $\pm$ 32.9 | 0.252   | 0.617            |
| 12        | 409.4 $\pm$ 34.3    | 413.0 $\pm$ 32.0 | 0.180   | 0.672            |
| 13        | 391.7 $\pm$ 32.4    | 396.5 $\pm$ 32.1 | 0.341   | 0.561            |
| 14        | 377.2 $\pm$ 30.4    | 381.9 $\pm$ 31.6 | 0.366   | 0.547            |
| 15        | 362.9 $\pm$ 29.8    | 366.9 $\pm$ 30.8 | 0.279   | 0.599            |
| 16        | 350.0 $\pm$ 28.8    | 353.1 $\pm$ 31.5 | 0.171   | 0.681            |
| 17        | 338.0 $\pm$ 27.9    | 341.2 $\pm$ 30.8 | 0.191   | 0.663            |
| 18        | 328.1 $\pm$ 27.4    | 329.3 $\pm$ 29.6 | 0.030   | 0.863            |
| 19        | 316.7 $\pm$ 27.1    | 318.7 $\pm$ 28.1 | 0.081   | 0.777            |
| 20        | 306.7 $\pm$ 26.5    | 308.7 $\pm$ 28.2 | 0.080   | 0.779            |
| 21        | 296.9 $\pm$ 25.8    | 298.5 $\pm$ 27.6 | 0.056   | 0.814            |

\* *p*-values were calculated using a general linear model after adjusting for the effects of gender, age and brain size.

**Table S7. Comparisons of network global efficiency between schizophrenic patients (SZ) and young normal controls (NC1).**

| Threshold | Mean Value $\pm$ SE |                    | F-value | $p$ -value* |
|-----------|---------------------|--------------------|---------|-------------|
|           | SZ (n=19)           | NC1 (n=24)         |         |             |
| 1         | 26.520 $\pm$ 0.292  | 27.685 $\pm$ 0.259 | 8.706   | 0.005       |
| 2         | 26.535 $\pm$ 0.274  | 27.672 $\pm$ 0.243 | 9.432   | 0.004       |
| 3         | 26.575 $\pm$ 0.262  | 27.637 $\pm$ 0.232 | 9.010   | 0.005       |
| 4         | 26.628 $\pm$ 0.267  | 27.590 $\pm$ 0.237 | 7.070   | 0.012       |
| 5         | 26.669 $\pm$ 0.253  | 27.549 $\pm$ 0.224 | 6.586   | 0.014       |
| 6         | 26.613 $\pm$ 0.237  | 27.571 $\pm$ 0.211 | 8.890   | 0.005       |
| 7         | 26.611 $\pm$ 0.229  | 27.558 $\pm$ 0.203 | 9.359   | 0.004       |
| 8         | 26.639 $\pm$ 0.226  | 27.494 $\pm$ 0.200 | 7.861   | 0.008       |
| 9         | 26.570 $\pm$ 0.249  | 27.490 $\pm$ 0.221 | 7.475   | 0.010       |
| 10        | 26.523 $\pm$ 0.249  | 27.468 $\pm$ 0.221 | 7.580   | 0.008       |
| 11        | 26.431 $\pm$ 0.241  | 27.439 $\pm$ 0.214 | 9.573   | 0.004       |
| 12        | 26.398 $\pm$ 0.247  | 27.365 $\pm$ 0.219 | 8.363   | 0.006       |
| 13        | 26.427 $\pm$ 0.249  | 27.220 $\pm$ 0.221 | 5.497   | 0.025       |
| 14        | 26.368 $\pm$ 0.258  | 27.165 $\pm$ 0.229 | 5.164   | 0.029       |
| 15        | 26.265 $\pm$ 0.230  | 27.120 $\pm$ 0.204 | 7.504   | 0.009       |
| 16        | 26.149 $\pm$ 0.235  | 27.104 $\pm$ 0.208 | 9.010   | 0.005       |
| 17        | 25.974 $\pm$ 0.229  | 27.152 $\pm$ 0.203 | 13.8    | 0.001       |
| 18        | 25.885 $\pm$ 0.233  | 26.983 $\pm$ 0.207 | 12.122  | 0.001       |
| 19        | 25.828 $\pm$ 0.230  | 26.797 $\pm$ 0.204 | 9.655   | 0.004       |
| 20        | 25.647 $\pm$ 0.232  | 26.781 $\pm$ 0.206 | 12.987  | 0.001       |
| 21        | 25.557 $\pm$ 0.237  | 26.690 $\pm$ 0.210 | 12.504  | 0.001       |

\*  $p$ -values were calculated using a general linear model after adjusting for the effects of gender, age, brain size and overall connectivity strength S.



**Table S8. Partial correlation coefficient (PCC) and correlation between global efficiency and cognition scores derived from 5-factor model of schizophrenic psychopathology over the whole range of connection threshold value.**

| Threshold | Cognitive scores |                 |
|-----------|------------------|-----------------|
|           | PCC              | <i>p</i> -value |
| 1         | -0.559           | 0.025*          |
| 2         | -0.558           | 0.025*          |
| 3         | -0.558           | 0.025*          |
| 4         | -0.562           | 0.024*          |
| 5         | -0.562           | 0.023*          |
| 6         | -0.568           | 0.022*          |
| 7         | -0.568           | 0.022*          |
| 8         | -0.567           | 0.022*          |
| 9         | -0.559           | 0.025*          |
| 10        | -0.574           | 0.020*          |
| 11        | -0.572           | 0.021*          |
| 12        | -0.576           | 0.020*          |
| 13        | -0.584           | 0.018*          |
| 14        | -0.567           | 0.022*          |
| 15        | -0.576           | 0.020*          |
| 16        | -0.592           | 0.016*          |
| 17        | -0.575           | 0.020*          |
| 18        | -0.572           | 0.021*          |
| 19        | -0.549           | 0.028*          |
| 20        | -0.593           | 0.016*          |
| 21        | -0.591           | 0.016*          |

\*Significant *p*-value ( $p < 0.05$ )

## References

- [1] Lindenmayer JP, Grochowski S, Hyman RB. Five factor model of schizophrenia: replication across samples. *Schizophr Res* 1995, 14: 229-234.
- [2] Lindenmayer JP, Bernstein-Hyman R, Grochowski S. A new five factor model of schizophrenia. *Psychiatr Q* 1994, 65: 299-322.