**Supporting Information**

**Table S1.** Pearson correlation coefficients of pairwise variables among demographic, clinical, and medication features

**Table S2.** Demographic and clinical characteristics in the study participants of TRS without CR

**Table S3.** Current dispositions and medications in the study participants of TRS without CR

**Table S4.** Adjusted z scores of d′ on Continuous Performance Test (CPT) in the study participants of TRS without CR.

**Table S1**. Pearson correlation coefficients of pairwise variables among demographic, clinical, and medication features†

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variable | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 |
| 1. Age | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 2. Age at onset | 0.39\*\*\* | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 3. Educational years | -0.19 | -0.09 | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 4. Illness duration | **0.65**\*\*\* | -0.44\*\*\* | -0.07 | 1 |  |  |  |  |  |  |  |  |  |  |  |  |
| 5. No. hospitalizations | -0.07 | -0.20\*\* | 0.03 | 0.09 | 1 |  |  |  |  |  |  |  |  |  |  |  |
| 6. CGI-S | 0.02 | -0.32\*\*\* | 0.05 | 0.29\*\*\* | 0.21\*\* | 1 |  |  |  |  |  |  |  |  |  |  |
| 7. Male sex‡ | -0.08 | -0.04 | 0.08 | -0.05 | -0.02 | 0.03 | 1 |  |  |  |  |  |  |  |  |  |
| 8. Early onset‡ | -0.28\*\*\* | **-0.55**\*\*\* | -0.06 | 0.19\*\* | 0.09 | 0.24\*\*\* | -0.03 | 1 |  |  |  |  |  |  |  |  |
| 9. Family history‡ | -0.05 | -0.18\*\* | 0.03 | 0.09 | 0.16\* | 0.10 | 0.02 | 0.19\*\* | 1 |  |  |  |  |  |  |  |
| 10. Cigarette-smoker‡ | -0.12 | 0.07 | -0.10 | -0.16\* | 0.08 | -0.17 | **0.50**\*\*\* | -0.08 | -0.10 | 1 |  |  |  |  |  |  |
| 11. Alcohol-user‡ | -0.08 | 0.03 | -0.03 | -0.10 | -0.12 | -0.03 | 0.19\*\* | -0.04 | 0.06 | 0.15\* | 1 |  |  |  |  |  |
| 12. Antipsychotic Dos. | -0.05 | -0.13 | 0.03 | -0.004 | -0.05 | 0.11 | 0.10 | -0.004 | -0.07 | 0.10 | 0.06 | 1 |  |  |  |  |
| 13. Chronic ward‡ | 0.13 | -0.14 | -0.04 | 0.27\*\*\* | 0.14\* | 0.38\*\*\* | -0.05 | 0.17\* | 0.002 | -0.16\* | -0.16\* | 0.09 | 1 |  |  |  |
| 14. Polypharmacy‡ | 0.06 | -0.01 | -0.02 | 0.07 | 0.04 | 0.14\* | 0.06 | -0.03 | -0.09 | -0.11 | 0.04 | **0.53**\*\*\* | 0.24\*\*\* | 1 |  |  |
| 15. Aty. antipsychotic‡ | -0.08 | -0.13 | 0.01 | 0.04 | 0.14\* | 0.22\*\* | -0.01 | 0.18\*\* | -0.10 | -0.08 | -0.06 | -0.36\*\*\* | 0.29\*\*\* | -0.15\* | 1 |  |
| 16. Clozapine user‡ | -0.03 | -0.26\*\*\* | -0.004 | 0.21\*\* | 0.27\*\*\* | 0.42\*\*\* | -0.02 | 0.24\*\*\* | 0.05 | -0.15\* | -0.12 | -0.17\* | **0.61**\*\*\* | 0.12 | 0.46\*\*\* | 1 |

CGI-S, Clinical Global Impression scale-Severity;

†the absolute value of correlation coefficient ≥ 0.5 in bold

‡binary variable

\*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001

**Table S2.** Demographic and clinical characteristics in the study participants of TRS without CR

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variables |  | Clozapine never-user (N=17) | |  | Clozapine responder (N=31) | |  | Group comparisons† |
|  |  | Mean | (SD) |  | Mean | (SD) |  | p |
| Age (years) |  | 48.4 | (9.8) |  | 44.0 | (8.2) |  | 0.1114 |
| Age of onset (years) |  | 23.8 | (9.6) |  | 21.8 | (6.3) |  | 0.4509 |
| Education (years) |  | 9.5 | (2.2) |  | 10.2 | (3.3) |  | 0.4447 |
| Illness duration (years) |  | 24.5 | (8.0) |  | 22.2 | (7.9) |  | 0.3353 |
| Number of hospitalizations |  | 3.8 | (3.3) |  | 5.3 | (3.1) |  | 0.1149 |
| CGI-S |  | 5.2 | (0.7) |  | 5.5 | (0.9) |  | 0.3179 |
|  |  | n | (%) |  | n | (%) |  | p |
| Male sex |  | 11 | (64.7) |  | 16 | (51.2) |  | 0.3818 |
| Early onset (onset age < 18 years) |  | 5 | (29.4) |  | 10 | (32.3) |  | 0.8388 |
| Family history of schizophrenia |  | 3 | (17.7) |  | 3 | (9.7) |  | 0.6513 |
| Current habitual cigarette-smoker |  | 10 | (62.5) |  | 12 | (38.7) |  | 0.1214 |
| Current habitual alcohol user |  | 0 | (0) |  | 0 | (0) |  | - |

TRS, treatment-resistant schizophrenia; CR, clozapine resistance; CGI-S, Clinical Global Impression scale-Severity.

†T-test for quantitative variables; χ2 test or Fisher’s exact test for categorical variables.

**Table S3.** Current dispositions and medications in the study participants of TRS without CR

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variables |  | Clozapine never-user (N=17) | |  | Clozapine responder (N=31) | |  | Group comparisons† |
|  |  | Mean | (SD) |  | Mean | (SD) |  | p |
| Current antipsychotic medications dosage, CPZE, (mg/day) |  | 656.3 | (405.7) |  | 349.8 | (218.8) |  | 0.0086 |
| Clozapine current dosage (mg/day) |  | - |  |  | 283.6 | (91.9) |  | - |
|  |  | N | (%) |  | N | (%) |  | p |
| Current disposition |  |  |  |  |  |  |  | 0.1694 |
| Chronic ward |  | 15 | (88.2) |  | 21 | (67.7) |  |  |
| Out-patient department |  | 2 | (11.8) |  | 10 | (32.3) |  |  |
| Acute ward |  | 0 | (0) |  | 0 | (0) |  |  |
| Polypharmacy |  | 6 | (35.3) |  | 9 | (29.0) |  | 0.6544 |
| Atypical-antipsychotic-user |  | 10 | (58.8) |  | 28 | (90.3) |  | 0.0220 |
| Clozapine use |  |  |  |  |  |  |  | < 0.0001 |
| Non-user |  | 17 | (100) |  | 0 | (0) |  |  |
| Ever-user |  | 0 | (0) |  | 2 | (6.4) |  |  |
| Current user |  | 0 | (0) |  | 29 | (93.6) |  |  |

TRS, treatment-resistant schizophrenia; CR, clozapine resistance; CPZE, chlorpromazine equivalent.

†T-test for quantitative variables; χ2 test or Fisher’s exact test for categorical variables.

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**Table S4.** Adjusted z scores of d′ on Continuous Performance Test (CPT) in the study participants with TRS without CR

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| CPT indicies |  | Clozapine never- user (N=17) | |  | Clozapine responder (N=31) | |  | Group comparisons |
| Continuous |  | Mean | (SD) |  | Mean | (SD) |  | p |
| Undegraded CPT |  |  |  |  |  |  |  |  |
| Adjusted z score of d′ |  | -4.57 | (1.70) |  | -2.62 | (2.79) |  | 0.0020† |
| Degraded CPT |  |  |  |  |  |  |  |  |
| Adjusted z score of d′ |  | -3.13 | (1.33) |  | -2.39 | (1.98) |  | 0.0695† |
| Binary |  | N | (%) |  | N | (%) |  | p |
| Undegraded CPT |  |  |  |  |  |  |  |  |
| Adjusted z score of d′ ≤ -2.5 (deficit) |  | 13 | (76.5) |  | 14 | (45.2) |  | 0.0365‡ |
| Degraded CPT |  |  |  |  |  |  |  |  |
| Adjusted z score of d′ ≤ -2.5 (deficit) |  | 12 | (70.6) |  | 18 | (58.1) |  | 0.3914‡ |

CPT, continuous performance test; TRS, treatment-resistant schizophrenia; CR, clozapine resistance; d′, the sensitivity index of performance on the CPT.

†ANCOVA for continuous variables with covariates including illness duration, number of hospitalizations, the scale of Clinical Global Impression-Severity, early onset or not, smoking status, current antipsychotic dosage, and atypical-antipsychotic-user or not.

‡χ2 test for categorical variables.