**Supplement**

# **Table S1.** *Descriptive characteristics of the discovery (N =57) and validation sample (N = 52).*

Statistics represent the comparison of the discovery and the validation sample. Abbreviations: DOI: duration of illness; CPZ: chlorpromazine equivalents; PANSS: Positive and Negative Syndrome Scale; CGI: Clinical Global Impression Scale; GAF: Global Assessment of Functioning Scale; *M:* mean; *SD*: standard deviation; *df*: degree of freedom. **χ2:** Chi square test; *t*: t statistic; *M-W-U.:* Mann-Whitney-U.

\**p* < .05;  \*\**p < .*01;\*\*\**p < .*001

#Mann-Whitney-U-test

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Discovery** | **Validation** | **Discovery vs Validation** |
|  | **(*N* = 57)** | ***(N* = 52)** | **ꭓ2** | ***(df)*** | ***P*** |
| **Gender (m : f)** | 47 : 10 | 28 : 24 | 10.37 | (1) | .001\*\* |
| **Hand preference (r : l : b)** | 52 : 4 : 1 | 43 : 7 : 2 | 1.78 | (2) | .411 |
| **Language (German : Other)** | 48 : 9 | 37:15 | 2.70 | (1) | .100 |
| **Smoker (y : n)** | 35 : 22 | 21 : 31 | 4.81 | (1) | .028\* |
|  | ***M*** | ***(SD)*** | ***M*** | ***(SD)*** | ***t /M-W-U*** | ***(df)*** | ***P*** |
| **Age** | 35.47 | (11.20) | 37.40 | (12.24) | 1358.50 |  | .453 |
| **Onset** | 26.29 | (8.61) | 26.46 | (10.56) | 1392.50 |  | .587 |
| **DOI** | 9.13 | (9.11) | 10.94 | (8.86) | 1249.50 |  | .158 |
| **CPZ** | 489.30 | (328.86) | 379.53 | (227.22) | 1188.50 |  | .075 |
| **School Years** | 11.37 | (2.14) | 11.47 | (2.74) | 1277.00 |  | .443 |
| **Cognition Index** | -0.48 | (0.67) | -0.22 | (0.57) | -2.22 | 107 | .029\* |
| **CGI** | 4.04 | (0.91) | 3.58 | (0.72) | 1052.00 |  | .008\*\* |
| **GAF** | 55.24 | (9.67) | 61.83 | (10.28) | -3.43 | 106 | <.001\*\*\* |
| **PANSS Total** | 61.89 | (16.56) | 48.44 | (11.58) | 732.00 |  | <.001\*\*\* |
| **PANSS Positive** | 14.20 | (5.65) | 11.35 | (3.50) | 1043.00 |  | .011\* |
| **PANSS Negative** | 17.00 | (5.07) | 12.17 | (4.76) | 647.50 |  | <.001\*\*\* |
| **PANSS General** | 30.70 | (8.34) | 24.92 | (5.61) | 844.00 |  | <.001\*\*\* |

# **Table S2.** *MPRAGE Scanning parameters*

Abbreviations:TR: Time of repetition; TE: echo time; FA: flip angle; slices, number of acquired slices

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Slices** | **Thickness** | **TE** | **TR** | **FA** | **resolution** |
| **Discovery sample** | 176 | 0.8 mm | 2.22 ms | 1900 ms | 9° | 0.8 × 0.8 × 0.8 mm |
| **Validation sample** | 256 | 0.75 mm | 2.17 ms | 2060 ms | 12° | 0.8 × 0.8 × 0.8 mm |

# **Supplement S3: Cognition Index**

**Table S3: Cognitive Measures**

|  |  |  |
| --- | --- | --- |
| **Test** | **Domain** | **Description** |
| VLMT | Episodic verbal memory | The investigator read out a list of 15 nouns five times (List A) and after each time participants had to recall as many nouns as possible (Trials 1-5). Afterwards, the investigator read out another list of 15 nouns (Interference List B), and participants recalled as many nouns as possible from List B. Next, participants had to recall the words from List A without further presentation immediately (trial 6) and after a 30 min delay (Trial 7). Lastly, the investigator read out a list with the words of List A, List B and 10 phonetically similar words to the words of List A and B (Recognition List W). After each word, the participants had to decide if it was in List A or not. *Measures:* as the sum of correct words during the learning phase (Trial 1 to 5), the decrease of learning performance after the 30 min. delay (Trial 5 minus Trial 7); and correct recognized List A words minus the errors (Trial W- F). |
| TMT-A | Motor speed | Participants had to connect the numbers 1 to 25 in a consecutive order as quickly as possible. *Measure*: time of task completion in s.  |
| DSST | Motor speed | Participants were asked to assign as many as possible symbols to numbers (1-9) according to a predefined coding scheme in 120 s. *Measure*: the number of correctly completed symbols (range: 0 – 133). |
| TMT-B | Cognitive flexibility | Participants had to connect the numbers 1 to 13 and the letters A to L in consecutive/alphabetical order, alternating between numbers and letters (e.g., 1-A-2-B). *Measure*: time of task completion in s. |
| DST | Working memory | During the DST the participants had to memorize and repeat numeric sequences forwards (DST forwards) or backward (DST backward). *Measure:* number of correct recalled numeric sequences forwards (range: 0 – 16) and backward (range: 0 – 14). |

The cognition index was constructed upon scores from VLMT (Sum of Trial 1 to 5, Trial 5 minus Trial 7, W - F), TMT (A and B, in s), DST (forwards and backward), and DSST (number of correct symbols) and calculations were based on the neurocognitive composite score described by Hasan et al. (2016). It included data from the discovery sample (*N* = 57*),* the validation sample *(N* = 52*)* and the normative sample *of* healthy controls and unaffected relatives (*N* = 74), and was constructed using SPSS in the following steps:

1. Recoding of variables: The variables VLMT Trial 5 minus VLMT Trial 7, TMT-A, and TMT-B were multiplied by -1 so that larger values would refer to a better performance.
2. Z-transformation: All variables were transformed into z-standard scores (with *M* = 0, *SD* = 1), to avoid influence of different scaling.
3. Calculation of cognition index: The cognition index was constructed as the weighted means of the z-scores using the formula:

$$Cognition index = \frac{1}{4}Mean\left(zVLMT\_{Sum\left(Trial 1 to Trial5\right) }, zVLMT\_{Trial5-Trial7}, zVLMT\_{W-F}\right) +$$

$$\frac{1}{4}Mean\left(zTMT\_{A}, zTMT\_{B}\right)+\frac{1}{4}zDSST + \frac{1}{4}Mean (zDST\_{forwards}, zDST\_{backward})$$

The cut-off value was defined as a 1.5 SD below the mean cognition index of the normative sample (*M* = 0.53, *SD* = 0.55) and thus at -0.29

# **Table S4.** *Comparison of the top 10 classification features of the two cognitive profiles (LowCog vs. HighCog) across the discovery (N = 57) and validation (N = 52) samples.*

Statistics represent the comparison of the HighCog and LowCog groups across both samples. Abbreviations: *M:* mean; *SD*: standard deviation; *df*: degree of freedom.; *t*: t statistic; *M-W-U:* Mann-Whitney-U statistic.

\**p* < .05; \*\**p < .*01;\*\*\**p < .*005

#Mann-Whitney-U-test

|  |
| --- |
| ***Discovery Sample (N* = 57*)*** |
|  | **HighCog (*n* = 25)** | **LowCog (*n =* 32)** |  |  |
|  | ***M*** | ***(SD)*** | ***M*** | ***SD*** | ***t (df) /******M-W-U#*** | ***p*** |
| Subcallosal gyrus (right) | 0.104 | (0.019) | 0.096 | (0.017) | -1.64 (55) | .106 |
| Transverse temporal sulcus (right) | 0.127 | (0.017) | 0.143 | (0.024) | 208.00# | .002\*\*\* |
| Inferior frontal sulcus (right) | 0.123 | (0.009) | 0.120 | (0.011) | -1.05 (55) | .299 |
| Inferior frontal sulcus (left) | 0.122 | (0.005) | 0.120 | (0.012) | 276.50***#*** | .047\* |
| Superior frontal sulcus (left) | 0.111 | (0.009) | 0.117 | (0.013) | 272.00***#*** | .039\* |
| Inferior occipital gyrus and sulcus (left) | 0.138 | (0.009) | 0.144 | (0.013) | 596.50***#*** | .038\* |
| Intraparietal sulcus and Precuneus transversal (left) | 0.116 | (0.006) | 0.115 | (0.012) | -0.64 (48.08) | .526 |
| Superior and transversal occipital sulcus (left) | 0.125 | (0.011) | 0.120 | (0.010) | -1.70 (55) | .095 |
| Long gyrus and Central sulcus of insula (right) | 0.151 | (0.016) | 0.144 | (0.018) | -1.51 (55) | .136 |
| Subcallosal gyrus (left) | 0.122 | (0.020) | 0.117 | (0.016) | 331.00***#*** | .267 |
| ***Validation Sample (N = 52)*** |
|  | **HighCog (*n* = 30)** | **LowCog (*n*  = 22)** |  |  |
|  | ***M*** | ***(SD)*** | ***M*** | ***(SD)*** | ***t (df) /******M-W-U#*** | ***p*** |
| Subcallosal gyrus (right) | 0.090 | (0.014) | 0.096 | (0.021) | 1.17 (50) | .247 |
| Transverse temporal sulcus (right)  | 0.125 | (0.021) | 0.120 | (0.016) | -0.97 (50) | .338 |
| Inferior frontal sulcus (right)  | 0.118 | (0.006) | 0.118 | (0.007) | 0.14 (50) | .891 |
| Inferior frontal sulcus (left) | 0.116 | (0.008) | 0.119 | (0.007) | 1.28 (50) | .207 |
| Superior frontal sulcus (left)  | 0.109 | (0.009) | 0.113 | (0.009) | 1.45(50) | .154 |
| Inferior occipital gyrus and sulcus (left)  | 0.141 | (0.009) | 0.136 | (0.006) | -2.32 (50) | .025\* |
| Intraparietal sulcus and Precuneus transversal (left) | 0.108 | (0.007) | 0.114 | (0.007) | 3.42 (50) | .001\*\*\* |
| Superior and transversal occipital sulcus (left)  | 0.115 | (0.009) | 0.121 | (0.010) | 2.06(50) | .045 |
| Long gyrus and Central sulcus of insula (right)  | 0.137 | (0.015) | 0.139 | (0.014) | 0.34 (50) | .737 |
| Subcallosal gyrus (left) | 0.108 | (0.021) | 0.109 | (0.016) | 0.30 (50) | .769 |