Neurophysiological and Psychological Predictors of Social Functioning in Patients with Schizophrenia and Bipolar Disorder

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Objective  The aim of this study is to examine social functioning in patients with schizophrenia and bipolar disorder and explore the psychological and neurophysiological predictors of social functioning.

Methods  Twenty-seven patients with schizophrenia and thirty patients with bipolar disorder, as well as twenty-five healthy controls, completed measures of social functioning (questionnaire of social functioning), neurocognition (Verbal fluency, Korean-Auditory Verbal Learning Test), and social cognition (basic empathy scale and Social Attribution Task-Multiple Choice), and the childhood trauma questionnaire (CTQ). For neurophysiological measurements, mismatch negativity and heart rate variability (HRV) were recorded from all participants. Multiple hierarchical regression was performed to explore the impact of factors on social functioning.

Results  The results showed that CTQ-emotional neglect significantly predicted social functioning in schizophrenia group, while HRV-high frequency significantly predicted social functioning in bipolar disorder patients. Furthermore, emotional neglect and HRV-HF still predicted social functioning in all of the subjects after controlling for the diagnostic criteria.

Conclusion  Our results implicated that even though each group has different predictors of social functioning, early traumatic events and HRV could be important indicators of functional outcome irrespective of what group they are.

Key Words  Social functioning, Schizophrenia, Bipolar disorder, Childhood trauma, Mismatch negativity, Heart rate variability.

INTRODUCTION

Social functioning, which refers to the degree to which a person adjusts to daily-life domains such as work and interpersonal relationship,¹,² has been regarded as a treatment outcome, as well as a diagnostic criterion, in psychiatric disorders. Previous studies have shown that patients with schizophrenia and bipolar disorder typically have poorer functioning than healthy controls.³,⁴ In particular, dimensional approaches have argued that schizophrenia and bipolar disorder patients have commonalities of clinical symptoms, family history, biological and genetic factors.⁶,⁸ This may suggest that both patient groups share similar predictors of impaired social functioning.

A large number of studies have investigated the relationship between cognitive impairment and social functioning in patients with schizophrenia and bipolar disorder.⁹,¹² In a recent meta-analysis,¹³ the association between verbal fluency and community functioning exhibited the largest effect size in schizophrenia patients. Moreover, a review stated that neurocognitive domains, such as verbal memory and executive function, are positively associated with psychosocial functioning in bipolar disorder patients, even after controlling for mood-related symptoms.¹⁴ In addition, social cognition, which includes emotional perception, social perception, theory of mind, and attributional style, has also shown a positive association with social functioning in bipolar patients, as well as schizophrenia patients.¹⁵,²¹
Furthermore, other studies have explored the relationship between traumatic childhood experiences and social functioning in schizophrenia and bipolar disorder.22,24 While the high prevalence of childhood trauma has been consistently reported in schizophrenia and bipolar disorder, the causal relationship between childhood traumatic events and social functioning has been explored recently. A previous study revealed that early trauma in psychosis patients affected long-term functional outcome, which was mediated by depressive symptoms. However, little is known about the specific relationship between early trauma and functional outcomes in bipolar disorder.30

In addition, neurophysiological factors may predict social functioning in schizophrenia and bipolar disorder. In this study, the mismatch negativity (MMN) and heart rate variability (HRV), which are considered as objective measures related to automatic responses and autonomic nervous system, were employed. Two of these markers have been long investigated as potential predictors of patient’s functional outcomes. MMN is an auditory event-related potential (ERP) component related to pre-attentive sensory memory. Recent findings have demonstrated that MMN is typically reduced in schizophrenia and bipolar disorder, and MMN deficits are associated with poor functioning in schizophrenia. Another notable factor is HRV, which is a reliable and quantitative measurement of autonomic nervous system activity. A growing number of studies have reported HRV dysfunction in schizophrenia and bipolar disorder. Previous studies have demonstrated that HRV is related to emotional regulation and emotion recognition. Fujibayashi and his colleagues reported that low functioning schizophrenia patients show reduced autonomic nervous system activities compared to high functioning group. Another study revealed that HRV predicts subjective well-being, mediated by executive emotional regulation, in college students.

In sum, even though a growing body of evidence has shown that cognitive impairments, childhood maltreatment, and neurophysiological factors are associated with functional outcomes in schizophrenia and bipolar disorder, few studies have examined the predictive effect of psychological and neurophysiological factors on the social functioning of both patients simultaneously. Therefore, the present study aimed to perform an exploratory examination of the predictor of social functioning, and the relationship between childhood traumatic experiences and social functioning has been explored recently.23,29 A previous study revealed that early trauma in psychosis patients affected long-term functional outcome, which was mediated by depressive symptoms. However, little is known about the specific relationship between early trauma and functional outcomes in bipolar disorder.

METHODS

Participants
A total of 82 subjects between the ages of 20 and 64 years participated in this study. The subjects included patients with schizophrenia [n=27, age: 42.48±11.86 (range: 21–60)] and bipolar disorder [n=30, age: 39.70±12.61 (range: 20–63)] as well as healthy controls [n=25, age: 42.48±12.60 (range: 23–64)]. All patients were assessed by a psychiatrist for Axis I disorders based on the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (SCID). Psychiatric symptoms were assessed using the Positive and Negative Syndrome Scale (PANSS) for patients with both diseases and the Young Mania Rating Scale (YMRS) for bipolar disorder. No patient had a lifetime history of central nervous system disease, alcohol or drug abuse, mental retardation, or head injury with loss of consciousness. Patients with schizophrenia were being treated with atypical antipsychotics, and patients with bipolar disorder with mood-stabilizing agents (lithium, topiramate, lamotrigine, and sodium valproate), with or without atypical antipsychotics. Twenty-five healthy controls were recruited from the local community through newspaper advertisements and flyers. Subjects with identifiable neurological disorders, head injury, or any personal or family history of psychiatric illness were excluded following an initial screening interview. Volunteers were then interviewed using the SCID for Axis II Psychiatric Disorders and excluded if they were found to have any disorder. All subjects signed a written informed consent form approved by the Institutional Review Board of Inje University Ilsan Paik Hospital (2015-07-23).

Psychological measures

Social functioning
To evaluate social functioning, the questionnaire of social functioning (QSF) was performed for all participants. The QSF consists of 16 items, which include frequency (8 items) and satisfaction (8 items) of social behaviors such as working and relationships, rated using a five-point Likert scale (ranging 1–5) where a higher score indicates greater social functioning. The Cronbach’s alpha for the current sample was 0.83.

Neurocognition
To assess neurocognition, a verbal fluency test and the Korean-Auditory Verbal Learning Test (K-AVLT) were employed. In the verbal fluency test, subjects state the names of as many animals as possible within 60 s. This evaluates verbal production and semantic memory abilities. The K-AVLT, which is included in the Rey-Kim Memory Test, is a verbal memory test consisting of five immediate recall trials (trials...
1–5), plus delayed recall and recognition trials. The immediate recall score is the sum of words (trials 1–5) recalled correctly. The delayed recall score indicates the number of words recalled correctly after a delay period of 20 min. The delayed recognition score involves indicating the chosen words in the original list (15 words) spoken by the examiner among a list of 50 words after delayed recall.

Social cognition
The Basic Empathy Scale (BES)\(^59\) and Social Attribution Task-Multiple Choice (SAT-MC)\(^60,61\) were used. The BES consists of 20 items rated using a five-point Likert scale (scoring 1–5), in which a higher score indicates higher empathic ability. The SAT-MC consists of a 64-s animation that shows a social drama played by a large triangle, small triangle, and small circle. The animation is shown twice, and 19 multiple-choice questions about the actions are answered by the participants after the second viewing. The Cronbach’s alpha for the BES in the current sample was 0.86.

Childhood trauma
Experience of childhood trauma was measured using the Childhood Trauma Questionnaire (CTQ)\(^62\). The CTQ consists of 28 items rated using a five-point Likert scale (scoring 1–5), in which higher scores indicate greater experience of childhood trauma. Subscales include physical, emotional, and sexual abuse, as well as physical and emotional neglect. Each subscale consists of five items, and an additional three items were utilized for validity, including minimization and denial. The Cronbach’s alpha for the CTQ in the current sample was 0.88.

Neurophysiological measures
Heart rate variability
HRV was measured using a 5-min single-channel (3-lead) electrocardiogram (ECG) signal. The ECG electrode sensors were attached to the left and right wrists and left ankle. After each subject was given approximately 5 minutes of rest in order to adapt to the experimental conditions, recordings were performed in the seated position at complete rest using the SA-3000P HRV analyzer (Medicore Co., Ltd, Seoul, Korea). The analyzer detected signals at 500 Hz, and the ECG signal was amplified and digitized. The following HRV parameters were calculated using frequency domain spectral analysis: low-frequency power (LF; 0.04–0.15 Hz), high-frequency power (HF; 0.15–0.4 Hz), and the LF/HF ratio. HF is considered an index of parasympathetic modulation, whereas LF is often proposed to reflect both sympathetic and parasympathetic activity.\(^63,64\) Furthermore, the LF/HF ratio can be used as a tool to assess cardiovascular autonomic regulation.\(^64\)

Recording and preprocessing of electroencephalography
The subjects were seated in a comfortable chair in a sound-attenuated room. They were required to watch a Charlie Chaplin movie displayed on a computer screen (Mitsubishi, 22-inch CRT monitor) without paying attention to the auditory stimuli. The auditory stimuli consisting of sounds at 85 dB SPL and 1000 Hz were delivered via MDR-D777 headphones (Sony, Tokyo, Japan). Deviant tones lasting 100 ms were presented randomly, interspersed with standard tones lasting 50 ms (probabilities: 10% and 90%, respectively). A total of 750 auditory stimuli were presented with an interstimulus interval of 500 ms. The experiment took about 10 min to complete. The stimuli were generated using E-Prime software (Psychology Software Tools, Pittsburgh, PA, USA).

EEG recording was synchronized to stimulus presentation onset by E-Prime. EEG data was recorded using 64 Ag-AgCl electrodes mounted on a Quik-Cap using an extended 10–20 placement scheme. The ground electrode was placed on the forehead and the physically linked reference electrodes were attached to both mastoids. The vertical electrooculogram (EOG) channels were positioned above and below the left eye, and the horizontal EOG channels were recorded from the outer canthus of each eye. The electrode impedance was kept below 5 kΩ. EEG data were assessed using a NeuroScan SynAmps amplifier (Compumedics USA, Charlotte, NC, USA) with a sampling rate of 1000 Hz and a 0.1–100 Hz band pass filter.

The recorded EEG data were preprocessed using CURRY 7 (Compumedics USA). A trained person with no prior information regarding the data origin removed gross artifacts such as movement artifacts by visual inspection. Artifact rejection related to eye movement or eye blinks was conducted using the mathematical procedure implemented in the preprocessing software of CURRY 7. The data were filtered using a 0.1–30 Hz bandpass filter and epoched from 100 ms pre-stimulus to 600 ms post-stimulus. The epochs were subtracted from the average value of the pre-stimulus interval for baseline correction. If any remaining epochs contained significant physiological artifacts (amplitude exceeding±75 μV) in any site over 62 electrodes, they were excluded from further analysis. Only artifact-free epochs were averaged across trials and subjects for ERP analysis. The MMN wave was generated by subtracting the standard ERP wave from the deviant ones. MMN amplitude was measured as the mean voltage between 130 and 280 ms at nine electrode sites (F3, Fz, F4, FC3, FCz, FC4, C3, Cz, and C4), because the frontocentral electrodes show larger MMN amplitudes. The time window for MMN amplitudes was based on visual in-
spection of the grand-averaged waveforms at FCz. The number of epochs of deviant and standard stimuli used in the analysis did not significantly differ between patients with schizophrenia or bipolar disorder and healthy controls (deviant stimuli: 65.96±6.55 vs. 66.90±7.10 vs. 67.60±9.13, p=0.739, standard stimuli: 589.56±60.20 vs. 596.47±62.96 vs. 604.56±82.07, p=0.733, respectively).

Statistical analysis
A chi-squared test and one-way analysis of variance (ANOVA) were employed to examine differences in demographic variables between the three groups. Preliminary analyses identified a non-normal distribution for HRV-LF and LF/HF ratio in the bipolar disorder group and for CTQ-sexual abuse in the healthy controls. As a result, log transformation was performed on these variables. Furthermore, MMN amplitudes at the nine electrodes were averaged to represent and interpret the results more suitably than using each electrode. A partial Pearson’s correlation analysis was conducted between QSF and other variables, including psychological measures, HRV, and MMN. For the patient groups, variables such as sex, age, duration of illness, and medication (i.e., equivalent doses of chlorpromazine and sodium valproate) were chosen as covariates based on the previous studies. For the healthy controls, age and sex were used as covariates. All factors significantly associated with the QSF (p<0.05) on the partial correlation analysis were included in a hierarchical multiple regression model. This was to identify significant predictors of social functioning in each group. Additionally, for exploratory purposes, the partial correlation analysis and the hierarchical regression analysis were performed with the data of all subjects. In this case, variables including group, sex and age were included as covariates. All analyses included a bias-corrected bootstrap 95% confidence interval (CI) based on 5,000 resampling. Statistical analyses were performed using SPSS 21 (IBM Corp., Armonk, NY, USA).

RESULTS

Demographic and psychological characteristics
Comparisons of demographic and psychological characteristics between the three groups are shown in Table 1. There were no significant differences with respect to sex, age, or education. The QSF scores were significantly lower in patients with schizophrenia and bipolar disorder than in healthy controls. Moreover, patients with schizophrenia and bipolar disorder showed significantly lower scores on verbal fluency and the K-AVLT (delayed recall, delayed recognition) than healthy controls. Furthermore, the scores of the SAT-MC were significantly lower in patients with schizophrenia and bipolar disorder than healthy controls. Regarding CTQ scores, patients with bipolar disorder showed significantly higher scores for physical abuse than schizophrenia patients and healthy controls. Additionally, patients with schizophrenia and bipolar disorder showed significantly higher scores for sexual abuse than healthy controls.

Neurophysiological measures: HRV and MMN
The ANOVA revealed no significant differences in HRV between the three groups. The average MMN amplitude for all nine channels for each group are shown in Table 1. The results revealed a significant main effect of group for average MMN (F=11.48, df=2, p<0.001). Post-hoc tests revealed that the patient groups showed significantly smaller MMN amplitudes than healthy controls (-1.51±0.98 μV, -2.12±1.38 μV, and -3.33±1.76 μV for schizophrenia, bipolar disorder, and healthy controls, respectively).

Correlations between QSF and other variables
Table 2 presents the results of the partial correlation analysis. In patients with schizophrenia, QSF was significantly correlated with HRV-LF/HF ratio and CTQ-emotional neglect. In patients with bipolar disorder, QSF was significantly correlated with HRV-HF. In healthy controls, QSF was significantly correlated with BES, CTQ-emotional neglect, and MMN. In all of eighty-two subjects, QSF was significantly associated with K-AVLT (delayed recall, delayed recognition), BES, CTQ-emotional neglect, physical neglect, and HRV-HF.

Multiple hierarchical regression analysis
Results of the hierarchical regression model in each group are presented in Supplementary Table 1, 2, 3 (in the online-only Data Supplement). In the schizophrenia group, CTQ-emotional neglect significantly predicted social functioning after controlling for sex, age, medication (CPZ, mood stabilizer), and duration of illness (B=-0.862, p=0.033). In the bipolar disorder group, HRV-HF significantly predicted social functioning after controlling for sex, age, medication (CPZ, mood stabilizer), and duration of illness (B=0.026, p=0.010). In healthy controls, MMN significantly predicted social functioning after controlling for sex and age (B=-2.072, p=0.033). Also, CTQ-emotional neglect and HRV-HF significantly predicted social functioning in all subjects (CTQ-emotional neglect: B=-0.477, p=0.023; HRV-HF: B=0.015, p=0.004) (Supplementary Table 4, in the online-only Data Supplement).

DISCUSSION
This study aimed to identify psychological and neurophys-
Table 1. Demographic characteristics of all study participants

|                      | Schizophreniaa (N=27) | Bipolar disorderb (N=30) | Healthy controlsc (N=25) | P     | Post-hoc (LSD) |
|----------------------|------------------------|--------------------------|--------------------------|-------|----------------|
| Age (years)          | 42.48±11.86            | 39.70±12.61              | 42.48±12.60              | 0.620 |                |
| Sex                  |                        |                          |                          | 0.704 |                |
| Male                 | 11 (40.7)              | 10 (33.3)                | 11 (44.0)                |       |                |
| Female               | 16 (59.3)              | 20 (66.7)                | 14 (56.0)                |       |                |
| Education (years)    | 13.52±2.56             | 12.33±3.71               | 14.24±3.27               | 0.620 |                |
| Number of hospitalizations | 3.22±3.86 | 4.34±10.66 | 0.092 | | |
| Duration of illness (years) | 11.22±7.70 | 10.10±6.81 | 0.562 | | |
| Onset age (years)    | 31.22±10.80            | 29.70±11.45              | 0.609 | | |
| Dosage of medication (CPZ equivalent, mg) | 518.58±657.94 | 343.33±475.04 | 0.251 | | |
| Dosage of medication (equivalent to sodium valproate dose, mg) | 83.33±250.00 | 752.57±443.20 | <0.001 | | |
| PANSS                |                        |                          |                          |       |                |
| Positive             | 13.78±8.49             | 9.37±3.01                | 0.015 | | |
| Negative             | 15.41±4.85             | 9.47±3.75                | <0.001 | | |
| General              | 30.63±10.32            | 24.40±6.72               | 0.011 | | |
| Total                | 59.81±21.59            | 43.23±11.87              | 0.001 | | |
| YMRS                 |                        |                          |                          |       |                |
| Verbal fluency       | 15.00±5.21             | 15.07±5.25               | 19.40±6.12               | 0.006 | a<c, b<c |
| KAVLT-trial 5        | 8.48±2.82              | 10.47±2.92               | 11.52±1.69               | <0.001 | a<b, a<c |
| KAVLT-delayed recall | 6.15±3.70              | 8.10±3.73                | 9.96±1.81                | <0.001 | a<b<c |
| KAVLT-delayed recognition | 10.44±2.98 | 11.77±2.66 | 13.92±1.26 | <0.001 | a<b<c |
| BES                  | 67.72±8.47             | 70.97±10.75              | 73.08±9.17               | 0.103 | | |
| SATMC                | 8.73±5.02              | 12.20±3.99               | 13.56±4.69               | <0.001 | a<c, b<c |
| CTQ                  |                        |                          |                          |       |                |
| Emotional abuse      | 9.11±4.85              | 10.30±5.41               | 8.00±4.20                | 0.225 | | |
| Physical abuse       | 8.63±3.62              | 11.03±5.61               | 8.04±2.78                | 0.024 | a<b, c<b |
| Sexual abuse         | 8.26±3.83              | 7.90±3.84                | 6.04±2.01                | 0.046 | c<a, c<b |
| Emotional neglect    | 11.00±5.14             | 13.53±6.10               | 10.92±3.67               | 0.099 | | |
| Physical neglect     | 8.48±3.20              | 9.80±4.05                | 7.68±3.25                | 0.087 | | |
| HRV                  |                        |                          |                          |       |                |
| LF                   | 209.50±214.66          | 187.03±273.17            | 275.53±262.59            | 0.416 | | |
| HF                   | 174.75±209.06          | 169.29±226.63            | 129.40±117.24            | 0.656 | | |
| LF/HF ratio          | 2.18±2.02              | 2.46±3.36                | 2.62±1.82                | 0.817 | | |
| MMN (total average)  | -1.51±0.98             | -2.12±1.38               | -3.33±1.76               | <0.001 | c<a, c<b |
| QSF                  | 49.33±9.34             | 48.70±11.19              | 55.20±6.90               | 0.027 | a<c, b<c |

CPZ: chlorpromazine, PANSS: Positive and Negative Syndrome Scale, YMRS: Young Mania Rating Scale, KAVLT: Korean Auditory Verbal Learning Test, BES: Basic Empathy Scale, SATMC: social attribution task-multiple choice, CTQ: childhood trauma questionnaire, HRV: heart rate variability, LF: low frequency, HF: high frequency, MMN: mismatch negativity, QSF: questionnaire of social functioning
significantly predicted functional outcome in all of eighty-two subjects after controlling for the diagnostic criteria.

Firstly, the social functioning of schizophrenia patients was negatively associated with HRV-LF/HF ratio and CTQ-emotional neglect. Further analysis revealed that only CTQ-emotional neglect was a significant predictor of social functioning. The increased HRV-LF/HF indicates the higher sympathetic nervous activity in comparison to parasympathetic nervous activity, which may result in less flexible autonomic system. In regard to the possible relation between HRV-LF/HF and stress regulation, an extensive review reported that an increase in the HRV-LF/HF ratio may reflect impaired stress regulation. This may insinuate the negative association between HRV-LF/HF ratio and social functioning in schizophrenia patients in our study. Also, previous studies have consistently shown a negative association between childhood trauma and functional outcomes in schizophrenia, as well as in high-risk offspring. For instance, Aas et al. reported that having a high prevalence of emotional neglect in childhood was associated with less improvement in global

Table 2. Partial Pearson’s correlations between QSF and neurocognition, social cognition, childhood trauma, HRV, and MMN (Bootstrapping=5000)

|                                | Patients with schizophrenia (N=27) |   | Healthy control subjects (N=25) |   |
|--------------------------------|------------------------------------|---|----------------------------------|---|
|                                | r       | p       |                                | r       | p       |
| QSF–Verbal Fluency             | 0.209   | 0.351   | QSF–Verbal Fluency             | 0.112   | 0.609   |
| QSF–KAVLT trial 5              | 0.173   | 0.441   | QSF–KAVLT trial 5              | 0.083   | 0.705   |
| QSF–KAVLT recall               | 0.241   | 0.281   | QSF–KAVLT recall               | -0.051  | 0.818   |
| QSF–KAVLT recognition          | 0.141   | 0.531   | QSF–KAVLT recognition          | -0.327  | 0.128   |
| QSF–BES total                  | 0.418   | 0.053   | QSF–BES total                  | 0.553   | 0.006   |
| QSF–SATMC                      | 0.203   | 0.364   | QSF–SATMC                      | 0.043   | 0.844   |
| QSF–CTQ_EA                     | -0.089  | 0.694   | QSF–CTQ_EA                     | 0.097   | 0.659   |
| QSF–CTQ_PA                     | 0.108   | 0.632   | QSF–CTQ_PA                     | -0.109  | 0.622   |
| QSF–CTQ_SA                     | 0.139   | 0.537   | QSF–CTQ_SA                     | -0.303  | 0.160   |
| QSF–CTQ_EN                     | -0.554  | 0.008   | QSF–CTQ_EN                     | -0.444  | 0.034   |
| QSF–CTQ_PN                     | -0.270  | 0.224   | QSF–CTQ_PN                     | 0.074   | 0.739   |
| QSF–HRV LF                     | -0.083  | 0.714   | QSF–HRV LF                     | 0.070   | 0.750   |
| QSF–HRV HF                     | 0.243   | 0.276   | QSF–HRV HF                     | -0.180  | 0.411   |
| QSF–HRV LF/HF                  | -0.448  | 0.037   | QSF–HRV LF/HF                  | 0.109   | 0.619   |
| QSF–total MMN                  | 0.190   | 0.396   | QSF–total MMN                  | -0.638  | 0.001   |

Patients with bipolar (N=30)

|                                | Patients with bipolar (N=30) |   | All participants (N=82) |   |
|--------------------------------|--------------------------------|---|------------------------|---|
|                                | r       | p       |                                | r       | p       |
| QSF–Verbal Fluency             | 0.067   | 0.750   | QSF–Verbal Fluency             | 0.155   | 0.174   |
| QSF–KAVLT trial 5              | -0.295  | 0.153   | QSF–KAVLT trial 5              | 0.054   | 0.639   |
| QSF–KAVLT recall               | 0.097   | 0.645   | QSF–KAVLT recall               | 0.238   | 0.035   |
| QSF–KAVLT recognition          | 0.249   | 0.231   | QSF–KAVLT recognition          | 0.268   | 0.017   |
| QSF–BES total                  | 0.145   | 0.490   | QSF–BES total                  | 0.241   | 0.032   |
| QSF–SATMC                      | -0.275  | 0.183   | QSF–SATMC                      | -0.022  | 0.846   |
| QSF–CTQ_EA                     | -0.278  | 0.179   | QSF–CTQ_EA                     | -0.199  | 0.078   |
| QSF–CTQ_PA                     | -0.250  | 0.229   | QSF–CTQ_PA                     | -0.156  | 0.169   |
| QSF–CTQ_SA                     | -0.379  | 0.062   | QSF–CTQ_SA                     | -0.178  | 0.117   |
| QSF–CTQ_EN                     | -0.111  | 0.597   | QSF–CTQ_EN                     | -0.300  | 0.007   |
| QSF–CTQ_PN                     | -0.101  | 0.630   | QSF–CTQ_PN                     | -0.243  | 0.005   |
| QSF–HRV LF                     | 0.285   | 0.167   | QSF–HRV LF                     | 0.171   | 0.131   |
| QSF–HRV HF                     | 0.558   | 0.004   | QSF–HRV HF                     | 0.311   | 0.005   |
| QSF–HRV LF/HF                  | -0.247  | 0.233   | QSF–HRV LF/HF                  | -0.045  | 0.694   |
| QSF–total MMN                  | -0.186  | 0.373   | QSF–total MMN                  | -0.217  | 0.055   |

The rows shaded in gray show the distinction among separate domains. The bold type highlights significant p-values (p=0.05). QSF: questionnaire of social functioning, KAVLT: Korean auditory verbal learning test, CTQ: childhood trauma questionnaire, EA: emotional abuse, PA: physical abuse, SA: sexual abuse, EN: emotional neglect, PN: physical neglect, BES: basic empathy scale, SATMC: social attribution task-multiple choice, HRV: heart rate variability, LF: low frequency, HF: high frequency, MMN: mismatch negativity.
functioning over course of one-year follow-up in a first-episode psychosis sample. In line with previous findings, our result shows that early emotional neglect could negatively affect social functioning in patients with schizophrenia. It would be advisable for clinicians to carefully elucidate any history of childhood abuse or neglect in patients with schizophrenia. In patients with bipolar disorder, the social functioning was significantly associated with HRV-HF. The HRV-HF remained a significant predictor of functional outcome in bipolar disorder. HRV-HF has been regarded as a measure of cardiac parasympathetic neural activity and a reflection of emotional regulatory capacity. Given that low variability in heart rate indicates abnormal or insufficient adaptability of the autonomic nervous system, reduced HRV-HF implies a difficulty in regulating one's emotional arousal, which could result in impaired functioning. It was reported that HRV is related to subjective well-being, mediated by executive emotion regulation. Other previous studies, which have shown the positive correlation between HRV-HF and social cognition, also support our results that HRV-HF is associated with social functioning. It seems that patients with reduced HRV-HF have difficulty in interpreting social information, which lead to impaired functioning. However, the result of our study did not show any significant differences in HRV parameters between the three groups, which is contrary to previous studies reporting that HRV in bipolar disorder is reduced relative to that in healthy controls. Considering that HRV in bipolar disorder was reduced during euthymia and depression compared to mania, the current affective state in bipolar disorder might affect difference in HRV. Our results suggest that to enhance functional outcomes in patients with bipolar disorder, interventions focusing on increasing adaptive emotional regulation would be needed. In healthy controls, social functioning was significantly associated with childhood trauma-emotional neglect, empathy, and MMN. Among those variables, MMN predicted functional outcomes in healthy controls. A significant association between emotional neglect and social functioning indicates that emotional support and security from a caregiver in childhood is important in acquiring social skills and forming relationships with others. Emotional neglect in childhood is known to influence social dysfunction in adulthood through the oxytocin level and attachment system in the general population. Empathic ability was also correlated with social functioning in healthy controls. A deficit in cognitive or emotional empathy could contribute to impairment in social functioning. Individuals with higher empathic ability were known to have larger social networks, which are associated with future life satisfaction and quality of life. On the other hand, lower empathic level is associated with depressive symptoms, which could result in poorer social functioning. Several studies have shown a significant association between deficit MMN and functional impairment in schizophrenia, as well as in healthy controls. Given that MMN reflects a predominantly automatic process, the present result indicates that neurophysiological measures assessing pre-attentive detection could be used as an indicator of functional outcomes in healthy controls. After controlling for the diagnostic criteria, CTQ-emotional neglect and HRV-HF still significantly predicted social functioning in all of eighty-two subjects. This result shows that early traumatic events strongly affect later functional outcome. The main implication for caregivers that can be drawn from this finding is the importance of emotional support and security during early childhood in preventing impaired functioning during adulthood. Also, HRV-HF could be used as a biological marker of social functioning level regardless of whether they are clinical or healthy control. Given that HRV-HF is an indicator of emotional self-regulation, emotional regulation training is expected to help people develop effective social interaction skills. Some limitations of the current study should be noted. Firstly, as subjective functioning measures were used, there is the possibility that patients' self-report would not reflect the objective evaluation of a clinician. Second, the sample size was relatively small, thus further a study with larger sample is needed to generalize our results. To conclude, our results suggest that social functioning in patients with schizophrenia and bipolar disorder, as well as healthy controls, could be associated with different neurophysiological and psychological factors. Additionally, emotional neglect in childhood and HRV-HF were significant predictors of functional outcome irrespective of what group they are, thus these factors should be regarded as important markers of social functioning.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.30773/pi.2019.07.28.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

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1. Burns T, Patrick D. Social functioning as an outcome measure in schizophrenia studies. Acta Psychiatr Scand 2007;116:403-418.
2. Stain HJ, Bennick K, Hegelstad WT, Joa I, Johansson JO, Langeveld J, et al. Impact of interpersonal trauma on the social functioning of adults with first-episode psychosis. Schizophr Bull 2013;40:1491-1498.
3. Cotter J, Kaeser M, Yung A. Childhood trauma and functional disability in psychosis, bipolar disorder and borderline personality disorder: a review of the literature. Ir J Psychol Med 2015;32:21-30.
4. Robertson BR, Prestia D, Twanmley EW, Patterson TL, Bowie CR, Harvey PD. Social competence versus negative symptoms as predictors of real world social functioning in schizophrenia. Schizophr Res 2014;160:136-141.
5. Simonsen C, Sundet K, Vaskinn A, Ueland T, Hellvin T, et al. Psychosocial function in schizophrenia and bipolar disorder: relationship to neurocognition and clinical symptoms. J Int Neuropsychol Soc 2010;16:771-783.
6. Daquetino C, De Rossi P, Spalletta G. Schizophrenia and bipolar disorder: the road from similarities and clinical heterogeneity to neurobiological types. Clin Chim Acta 2015;449:49-59.
7. Keshavan MS, Morris DW, Sweaney JA, Pearlson G, Thaker G, Seidman LJ, et al. A dimensional approach to the psychosis spectrum between bipolar disorder and schizophrenia: the Schizo-Bipolar Scale. Schizophr Res 2011;133:250-254.
8. Ketter TA, Wang PW, Becker OV, Nowakowska C, Yang YS. Psychotic bipolar disorders: dimensionally similar to or categorically different from schizophrenia? J Psychiatr Res 2004;38:47-61.
9. Bowrie CR, Depp C, McGrath JA, Wolyniec P, Mausbach BT, Thornquist MH, et al. Prediction of real-world functional disability in chronic mental disorders: a comparison of schizophrenia and bipolar disorder. Am J Psychiatry 2010;167:1116-1124.
10. Burdick K, Goldberg J, Harrow M. Neurocognitive dysfunction and psychosocial outcome in patients with bipolar I disorder at 15 year follow up. Acta Psychiatr Scand 2010;122:499-506.
11. Green MF. Cognitive impairment and functional outcome in schizophrenia and bipolar disorder. J Clin Psychiatry 2006;67(Suppl 9):3-8; discussion 36-42.
12. Martínez Aran A, Vieta E, Torrent C, Sanchez Moreno J, Goldkule J, Salamero M, et al. Functional outcome in bipolar disorder: the role of clinical and cognitive factors. Bipolar Disord 2007;9:103-113.
13. Fett A-KJ, Viechtbauer W, Penn DL, van Os J, Krabbendam L. The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: a meta-analysis. Neurosci Biobehav Rev 2011;35:573-588.
14. Wingo AP, Harley PD, Baldessarini RJ. Neurocognitive impairment in bipolar disorder patients: functional implications. Bipolar Disord 2009;11:113-125.
15. Couture SM, Penn DL, Roberts DL. The functional significance of social cognition in schizophrenia: a review. Schizophr Bull 2006;32(suppl 1):S44-S63.
16. Green MF, Horan WP, Lee J. Social cognition in schizophrenia. Nat Rev Neurosci 2015;16:620-631.
17. Hooker C, Park S. Emotion processing and its relationship to social functioning in schizophrenia patients. Psychiatry Res 2002;112:41-50.
18. Lahera G, Herrera S, Reinares M, Remoto A, Rullas M, González Cases J, et al. Hostile attributions in bipolar disorder and schizophrenia contribute to poor social functioning. Acta Psychiatr Scand 2015;131:472-482.
19. Lee S, Kim S, Chung Y, Park Y, Kim J. Neurocognition, Social Cognition and Functional Outcomes of Schizophrenia Patients. Oxford: Schizophrenia Bulletin; 2007.
20. Thorne U, Behere RV, Praharaj SK, Sharma PSVN. Facial emotion recognition, socio-occupational functioning and expressed emotions in schizophrenia versus bipolar disorder. Psychiatry Res 2018;264:354-360.
21. Vlad M, Raucher-Chêne D, Henry A, Kaladjian A. Functional outcome and social cognition in bipolar disorder: is there a connection? Eur Psychiatry 2018;52:116-125.
22. Alameda I, Ferrari C, Baumann P, Gholam-Rezaee M, Do K, Conus P. Childhood sexual and physical abuse: age at exposure modulates impact on functional outcome in early psychosis patients. Psychol Med 2015;45:2727-2736.
23. Andrianarisoa M, Boyer L, Godin O, Bruneel L, Bulzacca E, Aouizerate B, et al. Childhood trauma, depression and negative symptoms are independently associated with impaired quality of life in schizophrenia. Results from the national FACE-SZ cohort. Schizophr Res 2017;185:173-181.
24. Schenkel LS, Spaulding WD, Dilillo D, Silverstein SM. Histories of childhood maltreatment in schizophrenia: relationships with premorbid functioning, symptomatology, and cognitive deficits. Schizophr Res 2005;76:273-286.
25. Fowke A, Ross S, Ashcroft K. Childhood maltreatment and internalized shame in adults with a diagnosis of bipolar disorder. Clin Psychol Psychother 2012;19:450-457.
26. Larsson S, Aas M, Klungsøy O, Agartz I, Mork E, Steen NE, et al. Patterns of childhood adverse events are associated with clinical characteristics of bipolar disorder. BMC Psychiatry 2013;13:97.
27. Xie P, Wu K, Zheng Y, Guo Y, Yang Y, He J, et al. Prevalence of childhood trauma and correlations between childhood trauma, suicidal ideation, and social support in patients with depression, bipolar disorder, and schizophrenia in southern China. J Affect Disord 2018;228:41-48.
28. Alameda L, Golay P, Baumann PS, Progin P, Mebdouhi N, Elowe J, et al. Mild depressive symptoms mediate the impact of childhood trauma on long-term functional outcome in early psychosis patients. Schizophr Bull 2016;43:1027-1035.
29. López-Mongay D, Ahuir M, Crosas J, Navarro JB, Monreal JA, Obiols JE, et al. The effect of childhood sexual abuse on social functioning in schizophrenia spectrum disorders. J Interpers Violence 2018 [Epub ahead of print].
30. Kim JS, Lee SH. Influence of interactions between genes and childhood trauma on refactoriness in psychiatric disorders. Prog Neuropsychopharmacol Biol Psychiatry 2016;70:162-169.
31. Näätänien R. Mismatch negavity (MMN): perspectives for application. Int J Psychophysiol 2000;37:3-10.
32. Pumpella J, Howorka K, Groves D, Chester M, Nolan J. Functional assessment of heart rate variability: physiological basis and practical applications. Int J Cardiology 2002;84:1-14.
33. Fujibayashi M, Matsumoto T, Kishida I, Kimura T, Ishii C, Ishii N, et al. Functional assessment of heart rate variability: physiological basis and practical applications. Int J Cardiology 2002;84:1-14.
34. Lee SH, Sung K, Lee KS, Moon E, Kim CG. Mismatch negativity is a stronger indicator of functional outcomes than neurocognition or the relationship to functional impairments in chronic schizophrenia. Am J Psychiatry 2012;169:1741-1743.
35. Chitty KM, Lagopoulos J, Lee KS, Hickie IB, Hermens DF. A systematic review and meta-analysis of proton magnetic resonance spectroscopy and mismatch negativity in bipolar disorder. Eur Neuropsychopharmacol 2013;23:1348-1363.
36. Jahshan C, Wynn JK, Mathis KI, Alshuler LL, Glahn DC, Green MF. Cross diagnostic comparison of duration mismatch negativity and P3a in bipolar disorder and schizophrenia. Bipolar Disord 2012;14:239-248.
37. Kim S, Jeon H, Jung KI, Kim YW, Im CH, Lee SH. Mismatch negativity...
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ty and cortical thickness in patients with schizophrenia and bipolar disorder. Schizophr Bull 2019;45:425-435.
39. Umbricht D, Krifjes S. Mismatch negativity in schizophrenia: a meta-analysis. Schizophr Res 2005;76:1-23.
40. Light GA, Braff DL. Mismatch negativity deficits are associated with poor functioning in schizophrenia patients. Arch Gen Psychiatry 2005;62:127-136.
41. Wynn JK, Sugar C, Horan WP, Kern R, Green MF. Mismatch negativity, social cognition, and functioning in schizophrenia patients. Biol Psychiatry 2010;67:940-947.
42. Henry BL, Minassian A, Paulus MP, Geyer MA, Perry W. Heart rate variability in bipolar mania and schizophrenia. J Psychiatr Res 2010;44:168-176.
43. Bassett D, Bear N, Nutt D, Hood S, Bassett S, Hans D. Reduced heart rate variability in remitted bipolar disorder and recurrent depression. Aust N Z J Psychiatry 2016;50:793-804.
44. Cohen H, Kaplan Z, Kotler M, Mittelman I, Osher Y, Bersudsky Y. Impaired heart rate variability in euthymic bipolar patients. Bipolar Disord 2005;5:138-143.
45. Chang HA, Chang CC, Kuo TB, Huang SY. Distinguishing bipolar II depression from unipolar major depressive disorder: differences in heart rate variability. World J Biol Psychiatry 2015;16:351-360.
46. Moon E, Lee SH, Kim DH, Hwang B. Comparative study of heart rate variability in patients with schizophrenia, bipolar disorder, post-traumatic stress disorder, or major depressive disorder. Clin Psychopharmacol Neurosci 2013;11:137-143.
47. Valkonen Korhonen M, Tarvainen MP, Ranta Aho P, Karjalainen PA, et al. Reduced heart rate variability in schizophrenia and bipolar disorder. Acta Psychiatr Scand 2016;133:44-52.
48. Williams DP, Cash C, Rankin C, Bernardi A, Koenig J, Thayer JF. Resting heart rate variability predicts self-reported difficulties in emotion regulation: a focus on different facets of emotion regulation. Front Psychol 2015;6:261.
49. Appelhans BM, Lucenko LJ. Heart rate variability as an index of regulated emotional responding. Rev Gen Psychol 2006;10:229-240.
50. Quintana DS, Guastella AJ, Oplar LA. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr Bull 1987;13:261-276.
51. Young RC, Biggs JT, Ziegler VE, Meyer DA. A rating scale for mania: the Young Mania Rating Scale (YMRS) for the Schizophrenia Outpatients (SOP) study. J Nerv Ment Dis 1990;178:281-286.
52. Billman GE. The LF/HF ratio does not accurately measure cardiac sympatho-vagal balance. Front Physiol 2013;4:26.
53. Usall J, Baró J, Marco J, Martínez A, et al. Social functioning in schizophrenia: what is the influence of gender? Eur J Psychiatr Res 2007;21:199-205.
54. Ochoa S, Usall J, Villalta-Gil V, Vilaplana M, Márquez M, Valdelomar M, et al. Influence of age at onset on social functioning in outpatients with schizophrenia. Eur J Psychiatr Res 2006;20:157-163.
55. Di Simplicio M, Costoloni G, Western D, Hansøn B, Taggart P, Harmen C. Decreased heart rate variability during emotion regulation in subjects at risk for psychopathology. Psychol Med 2012;42:1775-1783.
56. Kim HG, Cheon EJ, Bai DS, Lee YH, Koo BH. Stress and heart rate variability: a meta-analysis and review of the literature. Psychiatry Invest 2018;15:235-245.
57. Aas M, Andreassen OA, Aminoff SR, Ferden A, Romm KL, Nesvag R, et al. A history of childhood trauma is associated with slower improvement rates: findings from a one-year follow-up study of patients with a first-episode psychosis. BMC Psychiatry 2016;16:126.
58. Berthelot N, Paccatello T, Gilbert E, Moreau I, Mérété C, Gingras N, et al. Childhood abuse and neglect may induce deficits in cognitive precursors of psychosis in high-risk children. J Psychiatry Neurosci 2015;40:336-343.
59. Gil A, Gama CS, de Jesus DR, Lobato MI, Zimmer M, Belmonte-de-Abreu P. The association of child abuse and neglect with adult disability in schizophrenia and the prominent role of physical neglect. Child Abuse Neglect 2009;33:618-624.
60. Lysaker PH, Meyer PS, Evans JD, Clements CA, Marks KA. Childhood sexual trauma and psychosocial functioning in adults with schizophrenia. Psychiatr Serv 2001;52:1485-1488.
61. Billman GE. Heart rate variability—a historical perspective. Front Physiol 2011;2:86.
62. Hughes JW, Stone CM. Depressed mood is related to high-frequency heart rate variability during stressors. Psychosom Med 2000;62:796-803.
63. Haegler M, Daniels JK, Lamke JP, Fydrich T, Walter H. Heart rate variability and its neural correlates during emotional face processing in social anxiety disorder. Biol Psychol 2013;94:319-330.
64. Bassett D. A literature review of heart rate variability in depressive and bipolar disorders. Aust N Z J Psychiatry 2016;50:511-519.
65. Faeh R, Jensen F, Almkvist O, et al. Development and validation of a brief screening version of the Developmental Trauma Questionnaire. Child Abuse Negl 2003;27:169-190.
66. Bernstein GD, Byte JA, Newcomb MD, Walker W, Pogge D, Ahluvalia T, et al. Development and validation of a brief screening version of the Childhood Trauma Questionnaire. Child Abuse Negl 2003;27:169-190.
ings from the ELSA study. J Aging Health 2015;27:919-934.
83. Bennik FC, Jeronimus BF, aan het Rot M. The relation between empa-
thy and depressive symptoms in a Dutch population sample. J Affect
Disord 2019;242:48-51.
84. Kupferberg A, Bicks L, Hasler G. Social functioning in major depres-
sive disorder. Neurosci Biobehav Rev 2016;69:313-332.
85. Light GA, Swedlow NR, Braff DL. Preattentive sensory processing as
indexed by the MMN and P3a brain responses is associated with cog-
nitive and psychosocial functioning in healthy adults. J Cogn Neurosci
2007;19:1624-1632.
86. Libby DJ, Worhunsky PD, Pilver CE, Brewer JA. Meditation-induced
changes in high-frequency heart rate variability predict smoking out-
comes. Front Hum Neurosci 2012;6:54.
87. Lopes PN, Salovey P, Côté S, Beers M, Petty RE. Emotion regulation
abilities and the quality of social interaction. Emotion 2005;5:113-118.
**Supplementary Table 1.** Hierarchical regression analysis predicting social functioning using BES and CTQ in patients with schizophrenia (N=27) (Bootstrapping=5000)

| Step | R²  | ΔR² | ΔF  | B      | t    | p    |
|------|-----|-----|-----|--------|------|------|
| 1.   | 0.135 | 0.135 | 0.652 | 1.151 | 0.276 | 0.770 |
| Sex  |       |      |       | 0.151  | 0.276 | 0.770 |
| Age  | -0.279 | -1.418 | 0.206 |        |      |      |
| Dosage of medication (CPZ) | 0.003 | 0.765 | 0.553 |        |      |      |
| Dosage of medication (mood stabilizer) | -0.011 | -0.925 | 0.296 |        |      |      |
| Duration of illness | 0.533 | 1.578 | 0.059 |        |      |      |
| 2.   | 0.487 | 0.353 | 6.536 | 0.897 | 0.265 | 0.780 |
| Sex  |       |      |       | 0.897  | 0.265 | 0.780 |
| Age  | -0.255 | -1.408 | 0.203 |        |      |      |
| Dosage of medication (CPZ) | 0.001 | 0.416 | 0.729 |        |      |      |
| Dosage of medication (mood stabilizer) | -0.005 | -0.540 | 0.567 |        |      |      |
| Duration of illness | 0.523 | 1.868 | 0.066 |        |      |      |
| HRV-LF/HF | -1.509 | -1.801 | 0.073 |        |      |      |
| CTQ-EN | -0.862 | -2.575 | 0.033 |        |      |      |

CPN: chlorpromazine, CTQ: childhood trauma questionnaire, EN: emotional neglect, HRV: heart rate variability, LF: low frequency, HF: high frequency
### Supplementary Table 2. Hierarchical regression analysis predicting social functioning using neurocognition, CTQ, and HRV in patients with bipolar disorder (N=30) (Bootstrapping=5000)

| Step | $R^2$ | $\Delta R^2$ | $\Delta F$ | B     | t     | p     |
|------|-------|--------------|------------|-------|-------|-------|
| 1.   | 0.299 | 0.299        | 2.045      | 0.108 | 0.453 | 0.637 |
| Sex  |       |              |            | 2.042 | -0.471|       |
| Age  |       |              |            | -2.628| -1.249| 0.016 |
| Dosage of medication (CPZ) | | | | -0.390 | -0.002 | 0.742 |
| Dosage of medication (mood stabilizer) | | | | -1.249 | -0.006 | 0.306 |
| Duration of illness | 0.767 | 2.354 | 0.035 |
| 2.   | 0.517 | 0.218        | 10.404     | 0.004 |       |       |
| Sex  |       |              |            | 3.702 | -0.308| 0.312 |
| Age  |       |              |            | -1.930| -0.308| 0.097 |
| Dosage of medication (CPZ) | | | | 0.274 | 0.001 | 0.798 |
| Dosage of medication (mood stabilizer) | | | | -1.903 | -0.007 | 0.087 |
| Duration of illness | 0.566 | 2.001 | 0.064 |
| HRV-HF | 0.026 | 3.226 | 0.010 |

CPZ: chlorpromazine, HRV: heart rate variability, HF: high frequency
**Supplementary Table 3.** Hierarchical regression analysis predicting social functioning using BES, CTQ, and MMN in healthy control subjects (N=25) (Bootstrapping=5000)

| Step | R²   | ΔR²  | ΔF    | B     | t    | p    |
|------|------|------|-------|-------|------|------|
| 1.   | 0.018| 0.018| 0.199 | 1.819 | 0.630| 0.546|
|      |      |      |       | Sex   |      |      |
|      |      |      |       | Age   | 0.000| 0.004| 0.996|
| 2.   | 0.574| 0.557| 8.281 | -1.052| -0.451| 0.677|
|      |      |      |       | Sex   |      |      |
|      |      |      |       | Age   | 0.010| 0.115| 0.910|
|      |      |      |       | BES   | 0.340| 2.135| 0.097|
|      |      |      |       | CTQ-EN| -0.295| -0.912| 0.356|
|      |      |      |       | MMN (total average) | -2.072 | -2.893 | 0.033|

CTQ: childhood trauma questionnaire, EN: emotional neglect, MMN: mismatch negativity
### Supplementary Table 4. Hierarchical regression analysis predicting social functioning using K-AVLT, BES, CTQ, and HRV in all subjects (N=82) (Bootstrapping=5000)

| Step | R²  | ΔR²  | ΔF  | B    | t    | p    |
|------|-----|------|-----|------|------|------|
| 1.   | 0.022 | 0.022 | 0.899 | 0.268 | 0.120 | 0.903 |
|      | Sex  | 0.268 | 0.120 | 0.903 | 0.903 |      |
|      | Age  | -0.119 | -1.339 | 0.199 | 0.199 |      |
| 2.   | 0.078 | 0.056 | 4.736 | 0.384 | 0.019 | 0.853 |
|      | Sex  | 0.384 | 0.019 | 0.853 | 0.853 |      |
|      | Age  | -0.120 | -0.150 | 0.200 | 0.200 |      |
|      | Group | 2.884 | 0.237 | 0.014 | 0.014 |      |
| 3.   | 0.332 | 0.254 | 4.557 | 0.245 | 0.123 | 0.889 |
|      | Sex  | 0.245 | 0.123 | 0.889 | 0.889 |      |
|      | Age  | -0.031 | -0.267 | 0.689 | 0.689 |      |
|      | Group | 1.405 | 0.978 | 0.274 | 0.274 |      |
|      | K-AVLT delayed recall | 0.584 | 1.598 | 0.149 | 0.149 |      |
|      | K-AVLT delayed recognition | 0.117 | 0.229 | 0.798 | 0.798 |      |
|      | BES  | 0.157 | 1.386 | 0.208 | 0.208 |      |
|      | CTQ-EN | -0.477 | -2.248 | 0.023 | 0.023 |      |
|      | CTQ-PN | -0.182 | -0.613 | 0.493 | 0.493 |      |
|      | HRV-HF | 0.015 | 2.851 | 0.004 | 0.004 |      |

K-AVLT: Korean Auditory Verbal Learning Test, BES: Basic Empathy Scale, CTQ: childhood trauma questionnaire, EN: emotional neglect, PN: physical neglect, HRV: heart rate variability, HF: high frequency