SOCIAL COGNITION AND QUALITY OF LIFE IN SCHIZOPHRENIA

Arija Maata, Anne-Kathrin J. Fett, Eske Derks and GROUP Investigators

DEPARTMENT OF PSYCHOLOGY AND EDUCATION, UNIVERSITY OF AMSTERDAM, AMSTERDAM, THE NETHERLANDS; DEPARTMENT OF EDUCATIONAL NEUROSCIENCE, UNIVERSITY OF Utrecht, Utrecht, The Netherlands; DEPARTMENT OF PSYCHOLOGY, ETH Zurich, Zurich, Switzerland; DEPARTMENT OF PSYCHOLOGY AND EDUCATION, UNIVERSITY OF AMSTERDAM, AMSTERDAM, THE NETHERLANDS.

1GROUP INVESTIGATORS: René S. Kahn (a), Don H. Linszen (b), Jim van Os (c,e), Durk Wiersma (d); Richard Bruggeman (d), Wiepke Cahn (a), Lieuwe de Haan (b), Lydia Krabbendam (c), Inez Myin-Germeys (c), (a) DEPARTMENT OF PSYCHOLOGY, RUDOLF MAGNUS INSTITUTE OF NEUROSCIENCE, UNIVERSITY MEDICAL CENTER UTRECHT, UTRECHT, THE NETHERLANDS; (b) DEPARTMENT OF PSYCHOLOGY, ACADEMIC MEDICAL CENTER, UNIVERSITY OF AMSTERDAM, AMSTERDAM, THE NETHERLANDS; (c) SOUTH LIMBURG MENTAL HEALTH RESEARCH AND TEACHING NETWORK, EURON, MAASTRICHT UNIVERSITY MEDICAL CENTER, MAASTRICHT, THE NETHERLANDS; (d) DEPARTMENT OF PSYCHOLOGY, UNIVERSITY MEDICAL CENTER GRONINGEN, UNIVERSITY OF GRONINGEN, GRONINGEN, THE NETHERLANDS; (e) KING’S COLLEGE LONDON, KING’S HEALTH PARTNERS, DEPARTMENT OF PSYCHOSIS STUDIES, INSTITUTE OF PSYCHIATRY, LONDON, UNITED KINGDOM.

ABSTRACT

Schizophrenia is associated with poor quality of life (QoL). Whereas the effects of neurocognitive deficits and psychopathology on QoL of schizophrenia patients have recently been elucidated, little is known about social cognitive deficits in this regard. This study investigated the influence of social cognition on QoL in schizophrenia. A sample of 1032 patients, 1011 of their siblings, and 552 healthy controls was recruited from the Dutch Genetic Risk and Outcome in Psychosis (GROUP) study. Participants completed a battery of cognitive tests, including social cognitive tests on theory of mind and emotion perception. To assess QoL the World Health Organization QoL Assessment-BREF (WHOQOL-BREF) was used. Schizophrenia symptoms were assessed with the Positive and Negative Syndrome Scale (PANSS). Social cognitive performance was significantly worse in patients compared to siblings and healthy controls. Patients had the poorest QoL, while QoL in healthy controls was better than in siblings. Theory of mind but not emotion perception or neurocognition was associated with QoL in patients, whereas neurocognition was the only significant predictor of QoL in siblings and healthy controls. There was a significant interaction between theory of mind and symptom severity with respect to QoL. Our study indicates that social cognition is associated with QoL in schizophrenia. Theory of mind rather than emotion perception is associated with QoL, and this association is moderated by schizophrenia symptoms. In particular, patients with relatively unimpaired theory of mind and more severe schizophrenia symptoms have poor QoL and, could therefore benefit from therapeutic intervention.

Keywords: Emotion Perception | Neurocognition | Schizophrenia | Social Cognition | Theory of Mind | Quality of Life
INTRODUCTION

Quality of life (QoL) in schizophrenia patients is impaired compared with that in the general population [1]. Clinical factors, including schizophrenia symptoms and neurocognitive functioning, and socio-demographic variables have been suggested to contribute to the poor life satisfaction of patients with this disorder [2-4]. However, the associations between neurocognition and QoL are fairly modest and some studies indicate that the association is non-significant when illness severity is taken into account [5-8]. Furthermore, the predictive role of socio-demographic variables appears to be minor [1]. QoL and functional outcome in patients with schizophrenia are related. The latter scores community functioning, whereas QoL measures subjective life satisfaction [9]. Evidence suggests that functional outcome in schizophrenia is more strongly related to social cognition than to neurocognition [10-12]. This raises the possibility that social cognition may be a factor influencing QoL in schizophrenia. To the best of our knowledge, this issue has not been studied so far. Therefore, the aim of the current study was to examine the relation of QoL and social cognition using a large group of schizophrenia patients.

Social cognition is a multidimensional construct [13]. Theory of mind (ToM) and emotion perception are important domains of social cognition based on the recent Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) recommendations [14]. ToM is the ability to infer the intentions and beliefs of others, sometimes also referred to as social intelligence [15]. Emotion perception is the ability to infer emotional information from facial expressions [13]. In this study, we focused on these two core domains of social cognition because they are impaired in schizophrenia and have previously been suggested to play a role in predicting outcome [10, 13]. ToM is probably the most important domain in this regard, as it is more strongly associated with community functioning \((r = 0.48)\), compared to other social cognitive domains including emotion perception \((r = 0.22)[10]\).

Although neurocognition and social cognition are separable domains [16], it has been argued that social cognitive impairment in schizophrenia is non-specific and that any association with outcome may be due to confounding by neurocognitive impairment [17-18]. Estimates of variance in social cognition accounted for by neurocognition range from 34% to 83% [19-20]. Importantly, most studies on the association of neurocognition and outcome do not report standardized measures of schizophrenia symptoms, thus neglecting the possibility that schizophrenia symptoms could moderate the relationship between cognition and outcome [21-23]. Therefore,
we included neurocognition and psychopathology in our analyses. In addition, we investigated the influence of social cognition and neurocognition on QoL of siblings of schizophrenia patients and of healthy controls to compare the effects of these factors on QoL between patients, their relatives and healthy individuals.

We hypothesized that social cognition of schizophrenia patients would predict their QoL. We expected that 1) the nature of the association would be positive, i.e. patients with a relatively unimpaired social cognition have a better QoL, and 2) ToM would more strongly predict QoL than emotion perception. To investigate an illness-related association, we explored a possible interaction between schizophrenia symptoms and social cognition in relation to QoL in patients.

**METHOD**

*Procedure and Sample*

The data derives from baseline measures of the ongoing longitudinal multicenter study ‘Genetic Risk and Outcome in Psychosis’ (GROUP). The procedure of recruitment, informed consent, approval by the accredited Medical Ethics Review Committee (METC) and population characteristics have been described in a previous report on the GROUP study [24]. The full GROUP sample consisted of 1120 patients with a non-affective psychotic disorder, 1057 of their siblings, 919 of their parents and 590 unrelated healthy controls from the general population. In the present study, we only included siblings of schizophrenia patients, because unlike the parents, they were raised under the same environmental conditions. Also, only the participants for whom an IQ score was available were included, because our aim was to include neurocognition in the analyses. Our inclusion criteria for patients, siblings and healthy controls were: 1) age between 16 and 60; 2) good command of the Dutch language and 3) ability and willingness to give informed consent. Patients had to meet the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [25] criteria for a non-affective psychotic disorder, as assessed by the Comprehensive Assessment of Symptoms and History Interview [26]. An additional inclusion criterion for the sibling group was the absence of a lifetime psychotic disorder. For the control group additional inclusion criteria were not having 1) a lifetime psychotic disorder and/or 2) a first degree family member with a lifetime psychotic disorder.
Measures

All the measures used in the GROUP project, were selected on the basis of established reliability and validity, as well as on their feasibility for use in large multisite studies.

1. Measure of Quality of Life

World Health Organization Quality of Life Assessment-BREF (WHOQOL-BREF). This instrument is a 26-item self-report questionnaire assessing QoL [27]. It includes four domain scores (physical, psychological, social and environmental) and two individually scored items measuring a subject’s overall perception of his QoL and satisfaction with his health. All items are rated on a five-point Likert scale. For all measures, higher scores reflect better QoL.

2. Measures of Social Cognition

Measure of Emotion Perception. The Degraded Facial Affect Recognition Task [28] uses photographs of four different actors (two male, two female) depicting four emotions: angry, happy, fearful and neutral. The task comprises 64 trials consisting of 16 face presentations in each emotion category. The emotions were shown with 75% intensity in order to increase the difficulty of the task. Subjects were asked to indicate the emotional expression of each face with a button press and to respond as accurately as possible. Outcomes were the proportion of faces correctly recognized as neutral, happy, fearful and angry emotions.

Measure of Theory of Mind. ToM was assessed with the Hinting Task [29-31]. The task tests the ability of subjects to infer the real intentions behind indirect speech utterances. It comprises ten short passages presenting an interaction between two characters that end with one of the characters dropping a hint. The subject is then asked what the character really meant. Correctly identified hints are scored with two points. In case of an incorrect response a more obvious hint is added. A subsequent correct response is scored with one point; an incorrect response is scored as zero. The outcome range is 0-20.

3. Measures of Neurocognition

Benton Facial Recognition Test. The short form of the Benton facial recognition test [32], a measure of the ability to match unfamiliar faces, was used to assess whether deficits in facial affect recognition are not mediated by differences in general facial recognition ability.
Wechsler Adult Intelligence Scale (WAIS III). The Arithmetic (working memory), Digit Symbol-Coding (processing speed), Block Design (reasoning and problem solving) and Information subtests (verbal comprehension) of the WAIS III were administered as an indicator of IQ [33-34]. We are aware that neurocognition in schizophrenia is often represented in terms of separable dimensions of cognitive deficits. Hence, the grouping of neurocognition as a single construct (IQ) is somewhat artificial. We did so in the current study to reduce the complexity of the models, minimize the number of parameters, and maximize the robustness of the findings.

4. Symptom Assessment

The Positive and Negative Syndrome Scale (PANSS). In the GROUP-project, current symptom severity was measured with the PANSS [35], which consists of 30 items. Each item is scored on a scale ranging from one (absent) to seven (extreme), with item rating incorporating the behavioural effect of symptoms as well as their severity. Three domains are described for the PANSS, measuring positive, negative or general symptoms. Since the current study did not emphasize symptom dimensions but rather the concept of clinical symptoms in relation to social cognition and QoL, we decided to calculate the mean score for every domain, allowing 30% missing values. The total of the mean sub-scores was used to assess the association between symptomatology and QoL in the current analyses.

Statistical Analyses

Statistical analyses were performed using SPSS version 15.0.

1. Sample Characteristics

Differences in QoL between schizophrenia patients, their siblings and healthy controls were evaluated with ANOVA. Differences in social cognition between groups may be subject to confounding by general neurocognitive performance, age and gender. Therefore, we evaluated the differences in social cognitive impairments with ANCOVA adjusted for IQ, age and gender. Performance on the facial affect recognition task was also adjusted for general face recognition ability. A type-I error rate of 0.05 was used for the between group comparisons.

2. Principal Component Analysis

As the QoL questionnaire contains four domains and two individually scored items, we sought to reduce these data to a single factor to minimize multiple testing. To investigate the underlying structure of the questionnaire, the data was subjected to
principal component analysis with varimax rotation. Prior to running the principal axis factoring, examination of the data on siblings and healthy controls indicated that the QoL-item measuring satisfaction with health was not perfectly normally distributed (skewness: -1.08). Given the robust nature of factor analysis, this deviation was not considered problematic.

3. Standard Multiple Regression

To determine whether social cognition was a predictor of QoL, we used standard multiple regression. For the patient group we also wanted to investigate the influence of illness severity on the analysis. Therefore, the total PANSS score (illness severity) was included as a predictor. In addition, we explored the interaction between illness severity and social cognition to examine possible interaction effects. All regression analyses were adjusted for the potentially confounding factors age, gender and IQ (for intercorrelations between IQ and the social cognitive tasks see Table 1). Prior to interpreting the results of the regression analyses, several assumptions were evaluated. Inspection of the normal probability plot of standardized residuals as well as the scatter plot for standardized residuals against standardized predicted values indicated that the assumptions of normality, linearity and homoscedasticity of residuals were met.

**Table 1 | Intercorrelations Between the (Social) Cognitive Tasks by Group (Pearson’s r)**

<table>
<thead>
<tr>
<th>Task</th>
<th>Controls</th>
<th>Siblings</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hinting</td>
<td>DFAR fearful</td>
<td>DFAR angry</td>
</tr>
<tr>
<td>DFAR fearful</td>
<td>0.03</td>
<td>0.05</td>
<td>0.17**</td>
</tr>
<tr>
<td>DFAR angry</td>
<td>0.07</td>
<td>0.28**</td>
<td>0.33**</td>
</tr>
<tr>
<td>IQ</td>
<td>0.16**</td>
<td>0.11**</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Note. DFAR = Degraded Facial Affect Recognition, **p < 0.001, *p < 0.05
RESULTS

The current study incorporated a subset of participants from the full GROUP sample. This subsample included 1032 schizophrenia patients, 1011 healthy siblings and 552 healthy controls. A total of 240 patients did not have a corresponding sibling included. The average number of siblings per patient that did have a relative included was 1.3. Sample characteristics are displayed in Table 2. Due to the family structure of the data, the data of patients and siblings was not statistically independent. We have tested whether this may possibly influence the results by calculating the correlations between patients and siblings for the main study-variables. The results of this analysis indicated that relatedness was not of major concern for a correct interpretation of the results, because the correlations were very weak (r ≈ 0.1). Because the siblings of the schizophrenia patients did not significantly differ from the healthy controls in their performance on the Hinting Task and the facial affect recognition task, we considered them as one group in further analyses, but we allowed for potential differences by including status (i.e. control vs. sibling) as a covariate in the multiple regression analyses. As shown in other studies examining differential responses to specific emotions [36-38], all groups recognized happy emotion best, followed by neutral, angry, and fearful emotion with the lowest rate of correct recognitions. Furthermore, in line with previous reports on affect recognition [39], schizophrenia patients only differed from the siblings and healthy controls in recognizing the negative emotions anger and fear. We only included these emotions in further analyses because of their apparent specificity to schizophrenia patients.
Table 2 | Demographic and clinical sample characteristics, group differences on QOL and group differences on social cognitive tests.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls</th>
<th>Siblings</th>
<th>Patients</th>
<th>Patients vs. Controls</th>
<th>Sibs vs. Controls</th>
<th>Patients vs. Sibs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 552</td>
<td>N = 101</td>
<td>N = 1032</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean (SD) n</td>
<td>Mean (SD) n</td>
<td>Mean (SD) n</td>
<td>Test statistic</td>
<td>p-value</td>
<td>p-value</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>29.6 (10.2)</td>
<td>27.9 (8.2)</td>
<td>27.3 (7.2)</td>
<td>F (2,2592) = 14.84</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Male (%)</td>
<td>46</td>
<td>77</td>
<td>77</td>
<td>( \chi^2(2) = 247.93 )</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>IQ</td>
<td>109.5 (15.0)</td>
<td>102.7 (15.5)</td>
<td>94.9 (16.0)</td>
<td>F (2,2592) = 165.68</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Illness Duration (yrs)</td>
<td>4.3 (4.0)</td>
<td>1.8 (1.1)</td>
<td>22.5 (6.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychotic episodes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age of onset (yrs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hinting Task</td>
<td>19.1 (1.3)</td>
<td>18.8 (1.7)</td>
<td>17.5 (2.8)</td>
<td>F (2,2551) = 40.48</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>DFAR neutral</td>
<td>81.5 (15.0)</td>
<td>80.4 (15)</td>
<td>77.8 (17.5)</td>
<td>F (2,2369) = 1.28</td>
<td>0.28</td>
<td>0.26</td>
</tr>
<tr>
<td>DFAR happy</td>
<td>87.3 (11.2)</td>
<td>88.2 (10.7)</td>
<td>86.8 (12.7)</td>
<td>F (2,2369) = 1.28</td>
<td>0.28</td>
<td>1.00</td>
</tr>
<tr>
<td>DFAR angry</td>
<td>70.4 (18.7)</td>
<td>68.8 (19.3)</td>
<td>62.5 (20.8)</td>
<td>F (2,2369) = 1.20</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>DFAR fearful</td>
<td>54.0 (18.2)</td>
<td>52.6 (19.7)</td>
<td>47.6 (19.7)</td>
<td>F (2,2369) = 7.57</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Benton</td>
<td>23.15 (2.1)</td>
<td>23.18 (2.2)</td>
<td>22.8 (2.3)</td>
<td>F (2,2537) = 1.94</td>
<td>0.15</td>
<td>1.00</td>
</tr>
<tr>
<td>PANSS positive</td>
<td>2.00 (0.86)</td>
<td></td>
<td>1.80 (0.76)</td>
<td></td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>PANSS negative</td>
<td>1.74 (0.52)</td>
<td></td>
<td>2.00 (0.86)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANSS general</td>
<td>5.54 (1.77)</td>
<td></td>
<td>5.14 (1.77)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANSS total</td>
<td>4.3 (0.6)</td>
<td>4.1 (0.7)</td>
<td>3.4 (1.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>QOL health</td>
<td>4.1 (0.8)</td>
<td>4.0 (0.9)</td>
<td>3.4 (1.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>QOL physical</td>
<td>4.2 (0.5)</td>
<td>4.1 (0.6)</td>
<td>3.4 (0.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>QOL psychological</td>
<td>3.8 (0.6)</td>
<td>3.6 (0.7)</td>
<td>3.2 (0.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>QOL social</td>
<td>4.0 (0.6)</td>
<td>3.9 (0.7)</td>
<td>3.2 (0.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>QOL environmental</td>
<td>4.1 (0.4)</td>
<td>4.0 (0.5)</td>
<td>3.5 (0.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


* Group differences on social cognitive tests and Benton adjusted for IQ, gender, age and face recognition ability (for DFAR only).
Principal Component Analysis of QoL

Data collected from patients (n = 930) and siblings and healthy controls (n = 1421) on QoL were subjected to principal component analysis. In both groups, one factor (with Eigenvalue exceeding 1) was identified as underlying the 26 questionnaire items. In total, this factor accounted for around 60% of the variance in the questionnaire data in the patient group and for around 59% in the ‘sibling and control’ group.

Standard Multiple Regression ‘Patients’

For the data on the group of schizophrenia patients, two regression analyses were performed. The first model was adjusted for the severity of symptoms measured by total PANSS score. The variables in the model (age, gender, IQ, total PANSS score and social cognition) explained 17% of the variability in QoL in patients, (F (7,805) = 24.16, p < 0.001). The Hinting Task was a significant predictor of QoL in this model (β = -0.09, p = 0.02). The performance on the Degraded Facial Affect Recognition Task did not significantly predict QoL. Importantly, contrary to the ‘sibling and healthy control’ group, IQ was not a significant predictor of QoL in schizophrenia patients (β = -0.03, p = 0.48). Post hoc analyses, in which we compared the effects of the separate PANSS scales in the regression, showed that all subscales had a negative effect on QoL, indicating that using the total PANSS score instead of separate scales was justified. Furthermore, because the sample consisted of recent-onset and chronic patients, a separate analysis was performed in which we included illness duration as a covariate. The results of this analysis were similar to those described above.

In our second model, we included an interaction effect of the Hinting Task and total PANSS score on QoL. We only included performance on the Hinting Task and not on the Degraded Facial Affect Recognition Task, because the Hinting Task performance had a significant main-effect in our first model and affect recognition did not. Table 3 shows that the interaction between total PANSS score and performance on the Hinting Task significantly predicted the QoL of patients. For the interaction factor the regression coefficient (β) was -0.36. By Cohen’s conventions, a combined effect of this magnitude can be considered ‘large’ (f² = -0.26) [40]. The model explained 17% of variance in QoL. We found that the total PANSS score was a moderator of the influence of the Hinting Task on QoL, as is graphically shown in Figure 1. The graph displays that in patients with a relatively low PANSS score, Hinting Task was not associated with QoL, while in patients with a mean or relatively high PANSS score a better performance on the Hinting Task was associated with a poor QoL.
Standard Multiple Regression ‘Siblings and Healthy Controls’

In siblings and healthy controls, variance in QoL could not be explained by performance on the Hinting Task or the Degraded Facial Affect Recognition Task (see Table 4). IQ uniquely accounted for variance in QoL, but in combination with the other variables, the model explained only 2.4% of the variability in QoL.

Table 3 | Unstandardised (B) and Standardised (β) Regression Coefficients for each Predictor in a Regression Model Predicting QoL for Patients including Interaction Variable (n = 812) (adjusted R² = 0.170).

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>95% CI</th>
<th>β</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.01</td>
<td>-0.02/-0.002*</td>
<td>-0.08</td>
</tr>
<tr>
<td>Gender</td>
<td>-0.04</td>
<td>-0.19/0.11</td>
<td>-0.02</td>
</tr>
<tr>
<td>IQ</td>
<td>-0.001</td>
<td>-0.01/0.003</td>
<td>-0.03</td>
</tr>
<tr>
<td>DFAR Angry</td>
<td>-0.001</td>
<td>-0.004/0.002</td>
<td>-0.03</td>
</tr>
<tr>
<td>DFAR Fearful</td>
<td>-0.003</td>
<td>-0.01/0.001</td>
<td>-0.06</td>
</tr>
<tr>
<td>Hinting Task</td>
<td>0.04</td>
<td>-0.03/0.11</td>
<td>0.12</td>
</tr>
<tr>
<td>Total PANSS</td>
<td>-0.05</td>
<td>-0.23/0.14</td>
<td>-0.09</td>
</tr>
<tr>
<td>(Total PANSS x Hinting Task)</td>
<td>-0.01</td>
<td>-0.02/-0.001*</td>
<td>-0.36</td>
</tr>
</tbody>
</table>

Note. QoL = Quality of Life. CI = confidence interval. DFAR = Degraded Facial Affect Recognition. PANSS = Positive and Negative Syndrome Scale. *p < 0.05.

Table 4 | Unstandardised (B) and standardised (β) regression coefficients for each predictor in a regression model predicting QoL for siblings and controls (n = 1323) (adjusted R² = 0.024).

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>95% CI</th>
<th>β</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.002</td>
<td>-0.004/ 0.01</td>
<td>0.02</td>
</tr>
<tr>
<td>Gender</td>
<td>-0.13</td>
<td>-0.24/-0.03*</td>
<td>-0.07</td>
</tr>
<tr>
<td>IQ</td>
<td>0.01</td>
<td>0.004/0.01 **</td>
<td>0.13</td>
</tr>
<tr>
<td>DFAR Angry</td>
<td>-9.37E-005</td>
<td>-0.003/0.003</td>
<td>-0.002</td>
</tr>
<tr>
<td>DFAR Fearful</td>
<td>-0.001</td>
<td>-0.004/0.002</td>
<td>-0.02</td>
</tr>
<tr>
<td>Hinting Task</td>
<td>0.03</td>
<td>-0.01/0.07</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Note. QoL = Quality of Life. CI = confidence interval. DFAR = Degraded Facial Affect Recognition. ** Inclusion of ‘group’ (‘sibling’ or ‘control’) in the analysis did not change the main finding of IQ as a significant predictor of QoL. *p < 0.05. **p < 0.001.

DISCUSSION

This study investigated the relationship between social cognition and QoL in schizophrenia taking into account neurocognitive functioning and schizophrenia symptoms. We show that social cognition, rather than neurocognition, is associated with QoL in schizophrenia. Moreover, we found that ToM is a more important domain of social cognition than emotion perception in relation to QoL of schizophrenia patients. The inclusion of symptomatology in our analyses revealed an interaction effect between symptom severity and ToM with respect to QoL. Schizophrenia symptoms appear to moderate the influence of ToM on QoL in such a way that more severely ill patients with a relatively unimpaired ToM have a poorer QoL. This illness-
related association is further emphasized by our finding that in siblings and healthy controls QoL is not related to social cognition but to neurocognition.

**Figure 1 | QoL in Schizophrenia Patients Adjusted for Total PANSS score (n = 887).**

The graph presents that in patients with a relatively low PANSS score, Hinting Task was not associated with QoL, while in patients with a mean or relatively high PANSS score a better performance on the Hinting Task was associated with a poor QoL. We divided the PANSS score in ‘high’ score (≥ mean +1 SD), ‘mean’ score (-1 SD > PANSS score < +1 SD) and ‘low’ score (≤ mean -1 SD) and plotted these three groups in a graph of QoL against the Hinting Task. Abbreviations: QoL = Quality of Life, QoL factor = standardized factor of Quality of Life. PANSS = Positive and Negative Syndrome Scale. low = PANSS score ≤ mean -1 SD. mean = -1 SD > PANSS score < +1 SD. high = PANSS score ≥ mean +1 SD.

**Quality of Life and Social Cognition**

In our study ToM but not neurocognition is significantly related to QoL of schizophrenia patients. This is in line with previous studies showing that social cognition is a stronger predictor of functional outcome in schizophrenia than neurocognition. However, whereas social cognition and functional outcome in schizophrenia are positively associated [10-12] we found ToM to be negatively associated with QoL. These different effects of social cognition may reflect the difference in outcome measures of QoL (subjective life satisfaction) and functional outcome (e.g. employment, housing and marital status). Apparently, whereas functional outcome in schizophrenia benefits from a higher social intelligence, QoL does not, probably because the patient realizes the impact of his illness on his social environment. The present findings are consistent with reports on relationships between QoL and ‘insight’ [41-42] and ‘social knowledge’ [5]. These studies point out, that patients with better insight and social knowledge recognize their illness-
related limitations, a recognition that is reflected in low QoL. ToM and insight in psychosis are related constructs, which may explain their similar effect on QoL in schizophrenia patients [43-45]. This assumption needs to be addressed in future research.

**Theory of Mind versus Emotion Perception**

Our study reveals that emotion perception is a less important domain of social cognition with respect to QoL in schizophrenia. A possible explanation could be that a correct understanding of the thoughts and intentions behind emotions (= ToM) is more important than reading emotions in facial expression (= emotion perception). For example, if a patient is able to recognize that his friend is angry or scared, this will not affect his QoL. However, if he is capable of recognizing that his friend is angry with him or scared of him because of his paranoid behaviour, this will increase his discomfort, resulting in impaired QoL.

**Quality of Life, Theory of Mind, and Schizophrenia Symptoms**

Intuitively, poor social cognition in schizophrenia patients should negatively affect QoL. Here, we find that poor ToM is inversely associated with QoL of a schizophrenia patient, on the condition that the patient has a relatively high total PANSS score. In other words, the relationship between social cognition and QoL is affected by the patient’s psychiatric distress. A possible explanation for the interaction between ToM and symptom severity is that more severely ill patients with a relatively unimpaired ToM may be aware of the detrimental effects of their illness on their social environment. Therefore, it is important that the social environment is aware of the status of a patients’ ToM, and understands that its interaction with the patient, can possibly negatively impact his well-being. Family coaching and education of peers could be helpful in this respect and help to improve QoL of schizophrenia patients.

**Strengths and Limitations**

The current study used a uniquely large sample to detect even delicate effects of the studied variables. The study was performed in the setting of daily psychiatric practice, which better reflects QoL in schizophrenia patients than clinical trials do. Also, as both a sibling and a healthy control group were added in the present study, we are certain that the association found between social cognition and QoL is specific to patients. Lastly, the inclusion of symptomatology in our analyses sheds
light on the confounding effect of symptoms on the association between social
cognition and QoL.

This study has limitations. First, the study is cross-sectional in design; hence, our
findings do not imply causality. To identify causality, longitudinal research on
symptoms, social cognitive functioning, and QoL in schizophrenia patients is needed.
Second, our finding of a non-significant difference in performance on Degraded
Facial Affect Recognition and Hinting Task between siblings and healthy controls is
not in line with previous studies, which demonstrated significant impairments in
siblings as well [29, 46]. One explanation for this lack of difference could be self-
selection bias, e.g. indicating that only the siblings with unimpaired social cognition
were willing to participate in our study. However, a different outcome of our model
was checked by using ‘sibling group’ or ‘healthy control group’ as a variable in
standard multiple regression and this did not change our findings. Furthermore, the
lack of an association between social cognition and QoL in siblings and healthy
controls should be interpreted with caution because of the nature of the employed
social cognitive task on ToM. The Hinting Task is specifically prone to ceiling effects
and this may partly account for the fact that we did not find an association.
Nevertheless, one could argue that all measures of ToM in non-psychotic siblings of
schizophrenia patients and healthy controls will have this limitation, because there is
by definition less variation in ToM among people without a psychotic disorder. Third,
our assessment of neurocognition only tapped into certain domains. Therefore, the
present conclusions do not necessarily generalize to all aspects of neurocognition.
Fourth, we are aware that the non-uniformity of the characteristics of our patient
sample with respect to patient status (clinically stable versus acutely ill) limits the
findings of our study. However, in order to keep the analysis as parsimonious as
possible, we limited our number of measures. Moreover, including duration of illness
in our analyses did not change our main findings. Lastly, there is some debate
regarding the capacity of people with a psychotic illness to make accurate
assessments of QoL [47]. However, validation studies demonstrate that self-report
measures of QoL are more accurate than clinician-report QoL measures, and that
QoL can be rated accurately by patients [48]. The results of the present study
indicate that schizophrenia patients with a relatively unimpaired ToM suffer from the
impact of their disease on the environment and warrant family-coaching to improve
patients’ QoL.
REFERENCES


