Towards an integrative approach to understanding quality of life in schizophrenia: The role of neurocognition, social cognition, and psychopathology

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Abstract

The term “schizophrenia” refers to a debilitating group of disorders that usually results in a severely impaired quality of life (QoL). Symptomatology appears to have a substantial role in determining QoL, although the relationship between QoL and specific psychotic symptoms is still unclear and has demonstrated mixed results. Due to the intrinsic importance of social functioning in QoL, and the mediating effect of social cognition on social functioning, the aim of this study was to try to investigate QoL in schizophrenia, not only in terms of symptomatology, but also in consideration of potential neurocognitive and social cognitive contributing factors.

Methods: Twenty-eight clinically stable patients with schizophrenia performed a broad range of neurocognitive and social cognitive assessments, and also participated in a semi-structured interview of QoL, assessing four partially independent subdomains of QoL. A stepwise regression model was used to determine the best predictors of QoL, and additionally a mediator analysis was performed to test for the mediating power of social cognition on QoL.

Results: Negative symptoms, intelligence, executive functioning and social cognition all had some power in predicting QoL in schizophrenia. Though most interestingly, mental state reasoning was specifically found to be most strongly related with the Intrapsychic Foundation subdomain of QoL, whereas neurocognition and symptom severity were associated with other subdomains of QoL.

Conclusions: The association between mental state reasoning and the more “internal” aspects of QoL in schizophrenia may reflect a specific role for social cognition in introspective and subjective judgments of one’s own QoL, whereas neurocognition and negative symptomatology may be more predictive of the external or extrinsic aspects of QoL. In conclusion, social cognitive skills appear to play a crucial role in the experience of one’s own subjective well-being, which could help to explain previous inconsistencies in the literature investigating QoL in schizophrenia.

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1. Introduction

Quality of life (QoL) is defined as “a multidimensional evaluation of an individual’s current life circumstances in the context of the culture in which they live and the values they hold” [1]. A wealth of studies have shown that subjective well-being, the prime measure of QoL, is severely compromised in patients with schizophrenia [2]. Put simply, the ultimate goal of remission in psychiatric illness is to improve quality of life.

In the past, symptom severity has been proposed to be the most important illness-related factor determining QoL in schizophrenia [3], however, the evidence for this assumption has received mixed empirical support. Norman et al. [4], for example, reported that patients who reported a greater subjective well-being expressed a lower severity of positive symptoms. However, on the other hand, others found lower negative symptoms to be more associated with better QoL [5], specifically in treatment-resistant patients receiving clozapine [6]. In addition, it has also been argued that
women tended to have fewer negative symptoms than men, which could explain the greater potential of the former to attain a better QoL in the social community [7,8]. Finally, a challenging study using both medicated and unmedicated patients with schizophrenia found no effect of the symptomatology on QoL [9], suggesting that the association between symptomatology and QoL is at best loose.

Recent research points to the fact that subjective well-being is not merely a matter of symptom reduction, but also heavily relies on neurocognitive functioning [10-13]. In support of this assumption, [14] reported that deficits in visual sustained attention, executive functioning, working memory and motor skills were found to be independent predictors of QoL, as measured by the Quality of Life Enjoyment and Satisfaction Questionnaire [15] and the Quality of Life Scale for Schizophrenia [16]. In their study, neurocognition explained 15% to 35% of the overall variance in QoL when severity of symptoms, medication effects and socio-demographical variables were controlled for. This has been supported by a recent meta-analysis demonstrating small to moderate effect sizes of verbal fluency, working memory, verbal list learning, processing speed, and executive functioning in predicting QoL [17]. In contrast to these findings, Heslegrave et al. [18] found no effect of visual sensory memory, perceptual span and visual processing on QoL. It is therefore plausible to assume that there may be other cognitive factors playing a role in mediating QoL in schizophrenia that have not been previously taken into consideration.

One candidate domain could be “social cognition”, which is defined as “the mental operations underlying social interactions” [19], and which has emerged as a critical mediator between neurocognition and functional outcome, as well as being a substantial predictor of social functioning [20-22]. Moreover, QoL has been shown to be highly associated with social functioning, thus sharing common ground in the macro social domain [23].

A recent factor analysis has identified three main domains of social cognition that are particularly impaired in schizophrenia (reviewed in [24]): (1) Emotion perception, which comprises of multiple impairments in emotion recognition from facial expression and prosody, emotion discrimination, and emotional awareness; (2) mental state reasoning and decoding, encompassing “theory of mind” (ToM) skills, that is, the ability to represent other people’s thoughts and intentions; (3) attributional style, referring to the tendency to whether negative or positive situations are causally attributed to oneself or to others.

To the best of our knowledge, only one study has sought to explore the specific role of social cognition in QoL in schizophrenia [25]. They found that neurocognition and mental state reasoning (ToM), as measured with the Hinting Task, were associated with QoL, whereas emotion perception was not. Importantly, both negative and positive symptomatology served as a mediating factor between ToM skills and QoL. Specifically, patients with preserved ToM skills and relatively high total PANSS scores tended to have a lower QoL, whereas those with preserved ToM and lower symptoms had a better QoL. However, their conclusion on the mediating role of negative symptoms is questionable as a substantial number of studies have concluded that social cognitive domains, including ToM skills, are independent from symptom clusters in schizophrenia, specifically from negative symptoms [13].

In sum, there is clearly a paucity of studies that take all possible predictors of QoL in schizophrenia into consideration, namely symptom severity, neurocognition and social cognition. Accordingly, the present study included measures of symptomatology, neurocognition and social cognitive performance comprising mental state reasoning and decoding, emotion perception and attributional style. We hypothesized that symptom severity, neurocognition, and social cognition would make independent contributions to predict QoL in schizophrenia, and that these domains would impact differentially on sub-categories of QoL.

2. Methods

2.1. Participants

Participants were 28 adult patients (13 men) with SCID confirmed DSM-IV diagnosis of schizophrenia. All participants were recruited from the Psychosis Unit of Celal Bayar University Psychiatry Department and were clinically stable. Exclusion criteria for all potential participants were having a known neurological disease, current substance abuse, mental retardation or acute psychotic episode in the last 6 months. The mean age was 24.14 ± 10.47 and education level 11.18 ± 3.18. Participants had, on average, lifetime psychiatric hospitalizations of 1.96 ± 1.93 years. Chlorpromazine equivalents were calculated for all patients in order to control for medication effects [26], and were 512 ± 361.43. All patients provided written informed consent. The study was approved by the local Institutional Review Board (Table 1).

2.2. Symptomatology (PANSS)

Symptom severity was measured with the Positive and Negative Syndrome Scale (PANSS; [27]). The PANSS is a 30-item semi-structured interview designed to assess five symptom categories associated with schizophrenia: positive symptoms (i.e., hallucinations and delusions), negative symptoms (i.e., avolition and anhedonia), cognitive symptoms (i.e., thought disorder), hostility, and depression. One trained and calibrated rater assigned a score from 1 to 7 for each item, with higher scores indicating more severe psychopathology.

2.3. Neuro-cognitive assessment

The Turkish versions of seven widely used neuropsychological procedures were used to evaluate seven basic cognitive domains, namely intelligence, executive
functioning, processing speed, attention, verbal memory and learning, visuo spatial memory. The tests were administered and scored by a trained psychiatrist (Z.C.) who was blind to the clinical data of the patients. More specifically, estimated intelligence was assessed with the Wechsler Memory Scale—III (WMS-III; [28]). Age corrected indices of the Memory functioning was measured with the Wisconsin Card Sorting Test-CV64 (WCST; [29]) number of correct answers and Trail Making Test (TMT; [30]) (Part B, connecting digits and letters) total time to completion. Processing speed was evaluated with the Trail Making Test (TMT; [30]) (Part A, letter sequencing) total time to completion. Attention was measured with the Continuous performance test [31] number of total correct responses. Verbal memory was measured with Rey Auditory Verbal Learning Test (RAVLT [32]; Rey. The total number of words recalled from the acquisition phase of the RAVLT (trials I–V) was used as an overall measure of verbal learning and recent verbal memory. Visuospatial memory was measured with the Benton the Judgment of Line Orientation test (Benton et al. [33].)

2.4. Social–cognitive assessment

The Turkish versions of five widely used social cognition procedures were used to evaluate three social cognitive domains, namely emotion perception, mental-state reasoning and attributional style. The performance tests were administered by a trained psychiatrist and then patients were rated by a psychiatrist and a psychologist together to improve accuracy and rule out interrater differences. Specifically, emotion perception was measured using the Face Emotion Identification Task (FEIT; [34]) using six basic facial emotion expressions (happiness, sadness, anger, fear, surprise, and ashamed,) presented on screen.

Mental state decoding was evaluated using the Reading-the-Mind-in-the-Eyes Test-Revised (RMET; [35]) which presents only the eye region of emotional faces on screen and participants choose which one of four emotions best describes what the person thinks or feels. Mental state reasoning was measured with the Hinting task [36], and the Unexpected Outcomes test (UOT; [37]). The Hinting Task, which measures the social–cognitive domain of the ToM, consists of ten brief written vignettes describing social hints that the participant is asked to interpret. Total number of correct responses scores ranges from 0 to 20, with higher scores indicating better performance. The Unexpected Outcomes Test consists of a 12-item measure of reasoning about the emotional states of others, and hence, reflects one’s empathic abilities.

Attributional style was measured with The Internal Personal and Situational Attributions Questionnaire (IPSAQ; [38]), which has 32 hypothetical social situations that are read to subjects and the subjects are then expected to make causal attributions. These attributions are classified as internal (related to self) and external (personal or situational). A bias made to internalize negative situations is calculated as the internalization bias (IB) whereas a bias to externalize negative situations is calculated as the externalization bias (EB).

2.5. Quality of life

The Quality of Life Scale (QLS; [16]) is a semi-structured interview to assess patients’ self-report and observers’ judgments about patient functioning and life circumstances. This instrument includes four subscales measured by a total of 21 items and each item is rated on a scale from 0 to 6. The four subscales are Interpersonal Relations, Instrumental Role, Intrapsychic Foundation, and Common Objects and Activities. Higher scores indicate higher levels of Quality of Life (QoL). An experienced psychiatrist (AED) who has treated the patients for long a period of time and understood the patients’ living conditions conducted the interviews according to the evaluation manual for the QLS [16].

2.6. Data analysis

After checking the data for the assumptions of linear analysis; in the first step, Pearson correlations were analyzed between the QoL subdomain total scores and age, duration of illness, education, mean treatment dose, PANSS subscales, neurocognitive tests and social cognitive tests. We hypothesized that the significant correlations identified possible predictors, and therefore in the second step, a stepwise multiple regression analysis was conducted with these possible predictors to determine the best predictors of QOL subdomains. Each variable was entered into the multiple regression analysis if its F value was >4. A p value <0.05 was
considered significant. Lastly, a mediator analysis was conducted following the guidelines of Baron and Kenny [39]. The best predictors from the previous stepwise regression analyses were included as independent predictors, whereas significant domains of social cognition were included as potential mediators in predicting QoL subdomains. Tree regressions were tested respectively: (1) domains of social cognition were regressed on the independent predictors from the previous step, (2) QoL subdomains were regressed on domains of social cognition and, (3) QoL was regressed on both social cognition and the independent predictors, therefore testing whether social cognition would still explain variance in addition to the independent predictors in the hierarchical multiple regression model. Perfect mediation would mean that an independent predictor has no effect on QoL when social cognition is included. If the first and/or the second regression is not significant, the last regression is not further conducted. Statistical analyses were performed using SPSS 19.0 software (SPSS Inc., Chicago, IL).

3. Results

Table 2 shows the correlations between QoL subdomains and independent predictors. Accordingly, the Interpersonal Relations subdomain of QoL was related to estimated intelligence, executive functioning, the cognitive domain of ToM, reasoning and negative symptoms. Instrumental Role was correlated with estimated intelligence, mental state reasoning and negative symptoms. Intrapsychic Foundation was associated with estimated intelligence, processing speed, verbal learning, mental state reasoning and both social and perceptual domains of ToM. Lastly, Common Objects and Activities were related to education, estimated intelligence, processing speed and negative symptoms.

Table 3 shows the results of the stepwise regression analysis on the QoL subdomains. The quality of Interpersonal Relations was significantly predicted by the negative symptoms and the estimated intelligence. The quality of occupational performance was significantly predicted by estimated intelligence. The quality of Intrapsychic Foundation was predicted by negative symptoms and mental state reasoning. Executive functioning and estimated intelligence predicted the Common Objects and Activities subdomain of QoL.

Lastly, according to the mediator analysis, social cognition did not show a potential mediating effect among all predictors and QoL subdomains.

4. Discussion

The present study sought to examine the predictive role of symptomatology, neurocognition and social cognition on QoL in schizophrenia. In essence, the results partially support our hypothesis of the independent role of social cognition on QoL. Specifically, mental state decoding was found to be a significant predictor of the Intrapsychic Foundation subdomain of QoL, which encompasses an individual’s reasoning and negative symptoms. Intrapsychic Foundation was associated with estimated intelligence, processing speed, verbal learning, mental state reasoning and both social and perceptual domains of ToM. Lastly, Common Objects and Activities were related with education, estimated intelligence, processing speed and negative symptoms.

Table 2
Correlational analyses between subdomains of QoL and their possible predictors.

<table>
<thead>
<tr>
<th></th>
<th>Interpersonal Relations</th>
<th>Instrumental Role</th>
<th>Intrapsychic Foundation</th>
<th>Common Objects and Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>.012</td>
<td>.086</td>
<td>.015</td>
<td>.096</td>
</tr>
<tr>
<td>Education (years)</td>
<td>.129</td>
<td>.178</td>
<td>.139</td>
<td>.382*</td>
</tr>
<tr>
<td>Duration of illness</td>
<td>-.051</td>
<td>-.048</td>
<td>.062</td>
<td>.163</td>
</tr>
<tr>
<td>Chlorpromazine Equivalent</td>
<td>.131</td>
<td>.117</td>
<td>.176</td>
<td>-.168</td>
</tr>
<tr>
<td>MQ</td>
<td>.474*</td>
<td>.537**</td>
<td>.496*</td>
<td>.478*</td>
</tr>
<tr>
<td>WCST number of correct responses.</td>
<td>-.012</td>
<td>.086</td>
<td>-.086</td>
<td>-.250</td>
</tr>
<tr>
<td>TMT-B (s)</td>
<td>-.462*</td>
<td>-.197</td>
<td>-.265</td>
<td>-.108</td>
</tr>
<tr>
<td>TMT-A (s)</td>
<td>-.342</td>
<td>-.294</td>
<td>-.454*</td>
<td>-.594**</td>
</tr>
<tr>
<td>Rey Auditory Verbal learning test</td>
<td>.358</td>
<td>.301</td>
<td>.394*</td>
<td>.315</td>
</tr>
<tr>
<td>Continuous performance test</td>
<td>.002</td>
<td>-.007</td>
<td>.052</td>
<td>.023</td>
</tr>
<tr>
<td>Line orientation test</td>
<td>.032</td>
<td>-.259</td>
<td>.034</td>
<td>.174</td>
</tr>
<tr>
<td>Face recognition test</td>
<td>.130</td>
<td>.166</td>
<td>.207</td>
<td>.215</td>
</tr>
<tr>
<td>Face discrimination test</td>
<td>.031</td>
<td>.060</td>
<td>.195</td>
<td>.160</td>
</tr>
<tr>
<td>Hinting task</td>
<td>.419*</td>
<td>.274</td>
<td>.492**</td>
<td>.060</td>
</tr>
<tr>
<td>ToM-Eyes test</td>
<td>.315</td>
<td>.069</td>
<td>.436*</td>
<td>.131</td>
</tr>
<tr>
<td>Unexpected outcomes test</td>
<td>.470*</td>
<td>.408*</td>
<td>.548**</td>
<td>.174</td>
</tr>
<tr>
<td>IPSAQ-Externalizing Bias</td>
<td>.287</td>
<td>.159</td>
<td>.306</td>
<td>.276</td>
</tr>
<tr>
<td>IPSAQ-Personalizing Bias</td>
<td>.090</td>
<td>-.104</td>
<td>.045</td>
<td>.055</td>
</tr>
<tr>
<td>PANSS Positive</td>
<td>-.281</td>
<td>-.201</td>
<td>-.174</td>
<td>-.248</td>
</tr>
<tr>
<td>PANSS Negative</td>
<td>-.616**</td>
<td>-.412*</td>
<td>-.576**</td>
<td>-.452*</td>
</tr>
<tr>
<td>PANSS General</td>
<td>-.360</td>
<td>-.340</td>
<td>-.359</td>
<td>-.122</td>
</tr>
</tbody>
</table>

*p = 0.05. **p = 0.01. P values indicated the significant correlations between QoL subdomains and predictors.
independently. In accordance with motivation, sense of purpose, curiosity, aimless inactivity, empathy and emotional interaction. In accordance with previous research, negative symptoms [7], intelligence [40,41], and executive functioning [18] were also found to predict QoL in schizophrenia.

When each domain of QoL is taken into account independently, the quality of occupational functioning is related to intelligence, whereas the quality of Interpersonal Relations, i.e. the relationship with the household, friends and having a social network, seems to be more strongly associated with the absence of negative symptoms. Executive functioning seems to have a specific predictive role in patients’ current daily activities such as reading a newspaper, paying the bills and common behaviors which can improve QoL like carrying a watch, wallet and ID card. Our results suggest that the Intrapsychic Foundation subdomain of QoL, which is determined by the internal motives for being an active member of the society, is closely related with mental state reasoning and decoding.

It is plausible to divide QoL into two main categories: one representing the outward (extrinsic) features of QoL, which include instrumental, interpersonal and daily activities; and the second representing the inward (intrinsic) features of QoL that relate to the subjective feeling of well-being. In light of this categorization, our results suggest that social cognitive skills such as mental state reasoning and decoding may be key predictors of the inward aspects of QoL, whereas neurocognitive faculties and negative symptoms may be more related with outward features. This is in line with work suggesting a relationship between the Intrapsychic Foundation domain of QoL and aspects of intrinsic motivation [42].

Importantly, other subdomains of social cognition, including emotion perception and attributional bias, were not associated with QoL in our study. Previous studies have implied an indirect relationship between a personalizing bias and perceived well-being, possibly caused by a potential association with self-stigmatization [43]. However, a personalizing bias may not be sufficient for self-stigmatization and therefore would not necessarily influence QoL [44]. Externalizing bias is related to suspiciousness and paranoid thoughts [45], and considering that our sample consisted of clinically stable patients, with less paranoid thoughts and negative symptoms, this may also explain why attributional style was not predictive of QoL.

With regard to the association between symptomatology and QoL, this study confirms previous accounts suggesting that negative symptoms predict QoL across sub-domains. Notably, our mediator analysis found no effect of social cognition in mediating predictors of QoL subdomains. This finding could conflict with work that has revealed a mediating role of social cognition on social functioning [46]. Since the negative symptoms on the PANSS include items that directly reflect social contact, this may inflate the relationships between QoL and psychopathology, and this strong relationship may consequently obscure the mediation effect of social cognition. Nevertheless, both social and neurocognition predicted some proportion of negative symptoms, as seen previously in many other studies [47,13]. Maat et al. [25] suggested that those patients with severe psychotic symptoms overall, but relatively preserved social cognition, may have good insight to their situation and therefore may actively withdraw from community life and consequently report a lower QoL. Comparing our results with this finding from Maat et al., it appears that poorer social cognitive and neurocognitive skills may have a detrimental effect on perceived self-competency and this may consequently reduce QoL scores in a clinically stable patient group, which is also in line with research linking metacognition with QoL [48]. In other words, it may be that a clinically stable patient group with less severe negative symptoms and impaired social cognitive abilities may make inaccurate judgments about their own competency. Therefore this would consequently have a negative impact on their own perception of their quality of life, i.e. the Intrapsychic Foundation domain of QoL. It is evident that the interdependent relationship between symptomatology, social cognition and QoL in schizophrenia may be deterministic and therefore it seems crucial to take a more holistic and integrative approach to understanding QoL when trying to see the bigger picture. Understanding the role of social cognition in QoL is important because, in line with our results and the literature, antipsychotic treatment does not seem to have a large effect on QoL [49]. If social cognition has an influence on QoL, then social cognition training could indirectly improve QoL. Social cognition has recently been

### Table 3
Stepwise multiple regression for subdomains of QoL.

<table>
<thead>
<tr>
<th>QoL subdomains</th>
<th>Predicting factors</th>
<th>F (df)</th>
<th>Partial R2</th>
<th>Model R2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interpersonal Relations</td>
<td>PANSS Negative</td>
<td>15.87 (2.27)***</td>
<td>.38***</td>
<td>.38</td>
</tr>
<tr>
<td></td>
<td>MQ</td>
<td></td>
<td>.12*</td>
<td>.50</td>
</tr>
<tr>
<td>Instrumental Role</td>
<td>MQ</td>
<td>10.53 (2.27)***</td>
<td>.29**</td>
<td>.29</td>
</tr>
<tr>
<td>Intrapsychic Foundation</td>
<td>PANSS Negative</td>
<td>11.70 (2.27)***</td>
<td>.33***</td>
<td>.33</td>
</tr>
<tr>
<td></td>
<td>Unexpected outcomes test</td>
<td></td>
<td>.15**</td>
<td>.48</td>
</tr>
<tr>
<td>Common Objects and Activities</td>
<td>TMT-B</td>
<td>10.75 (2.27)***</td>
<td>.35***</td>
<td>.35</td>
</tr>
<tr>
<td></td>
<td>MQ</td>
<td></td>
<td>.11**</td>
<td>.46</td>
</tr>
</tbody>
</table>

*p = 0.05, **p = 0.01 ***p = 0.005. P values indicate the significance of each model (F(df) column) and the contribution of each variable (partial R2 column) independently.
shown to be improved by psychosocial interventions [50]. For example, a recent study from our group found that remediation training that specifically targeted social cognition significantly improved patients’ self-reports of all subdomains of QoL [51]. This is promising in light of previous findings suggesting that cognitive remediation on neurocognition does not improve QoL in schizophrenia [52]. Our findings could have important clinical implications for the development of future psychosocial training for social cognition that could potentially have a substantial impact on improving QoL.

The study has several limitations. First, the correlational nature of this study precludes drawing firm conclusions with regards to causality. Second, the results found with our group of clinically stable patients with schizophrenia may not be generalizable to other stages of the disorder.

To sum up, to our knowledge this is the first study on the role of symptomatology, neurocognition and social cognition in QoL in schizophrenia. It underscores previous findings on the role of neurocognition and symptomatology but also highlights the specific role of mental state reasoning on QoL in schizophrenia.

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References