

The model of the relationships among the predictors of quality of life in chronic stage of schizophrenia

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ABSTRACT

We attempted to formulate a model of quality of life (QoL) in chronic stage of schizophrenia with 72 patients by including key variables, i.e., psychopathology, insight, executive functioning, and side effects, proposed to be its significant predictors in previous studies. We applied the structural equation modelling (SEM) method to simultaneously test a number of possible hypotheses concerning the inter-relations among the predictors of QoL in schizophrenia patients by formulating possible models and examining their levels of fitness. Our most fit model ($X^2=2.106$, $df=4$, $P=0.716$; CFI=1.000; TLI=1.213; RMSEA=0.000, LO=0.000, HI=0.132) showed that the severity of psychopathology not only directly causes poor QoL, but also by adversely affecting insight. On the other hand, executive function may not be affected significantly by psychopathology, but executive function still plays an important role in determining the QoL not only directly, but also indirectly by influencing self-evaluation of side-effects. Impaired insight and executive function caused by severe level of psychopathology contribute to an increased reporting of side-effects, resulting in cumulative dysfunction in daily life for patients with chronic schizophrenia. Our study illustrates that the complexity of the relationships among the predictors of QoL in chronic patients of schizophrenia should be considered when designing studies on QoL of this group.

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1. Introduction

Schizophrenia is an illness marked by heterogeneity not only in its aetiology, course, and outcome, but also in its psychopathological characteristics and related clinical variables, such as cognitive function and insight. Hence, while much effort has been placed thus far on identifying and delineating the linkages among psychopathology, clinical variables and outcome measures, inconsistent results have been often attributed to heterogeneity of patient samples. Unfortunately, however, many linkage approaches to quality of life (QoL) in patients of schizophrenia have also shared inconsistencies to which authors have cited differences in stage of illness (Karow et al., 2005;

Melle et al., 2005), treatment setting (Browne et al., 1996), and type of measures used (Lysaker et al., 2006; Whitty et al., 2004; Fitzgerald et al., 2003; Dickerson et al., 1998) as possible causes. In fact, Eack and Newhill (2007) through their meta-analysis have specifically found operationalization of QoL, study design, sample, and treatment setting to be moderating variables which could account for the variations in the effect sizes of QoL studies.

Moreover, as some clinical variables, such as treatment setting and stage of illness, may be significantly associated with and even interact with variables linked with QoL, such as side effects and cognitive functioning, it can be inferred that different patterns of relationship among the predictors of QoL may be found for various subgroups of patients. Hence, any one single model of QoL may not be suitable for all subgroups of patients. This has been supported by Karow et al. (2005) who argued for the need for a differential analysis of schizophrenia and QoL, because their longitudinal results have shown different patterns of relationship between psychopathology and various domains of QoL according to different phases of illness and treatment setting. Hence, development and validation of a reliable model of QoL for a relatively homogenous subgroup of patients can be a worthwhile venture, which may invariably facilitate research on improving medical services and assessing treatment effects and help formulate more appropriate policies for that target group.

Abbreviations: AGFI, adjusted goodness of fit index; BPRS, Brief Psychiatric Rating Scale; CFI, comparative fit index; EXIT, Executive Interview; LUNSERS, Liverpool University Neuroleptic Side Effects Rating Scale; QLS, Heinrichs Quality of Life Scale; QoL, quality of life; RMSEA, root mean square error of approximation; SEM, structural equation modeling; SUMD, Scale to Assess Unawareness of Mental Disorder; TLI, Tucker–Lewis Index.

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In this study, we attempted to formulate a model of QoL in chronic stage of schizophrenia by including key variables proposed by previous literature to be its significant predictors. Chronic stabilized patients were chosen because their symptoms are less volatile and the relationships among the clinical variables can be presumed to be more stable than those of acute-stage patients. Also, improving QoL may be as important as ameliorating psychopathological symptoms as treatment target for these patients, because poor QoL is likely to be a detrimental risk factor for certain crucial outcome variables. For example, about 20–40% of schizophrenia patients make suicide attempts (Pompili et al., 2007; Landmark et al., 1987; Planasky and Johnston, 1971) and rate of suicide deaths is about 10–13 times higher than general population (Caldwell and Gottesman, 1990, 1992). The significance of these figures become more apparent in light of the finding that dissatisfaction with greater number of life domains has been linked with repeated attempts at suicide (Ponizovsky et al., 2003).

Variables we have included in this study were psychopathology, insight, executive functioning, and side effects, whose overall model of inter-relationships in predicting QoL in chronic schizophrenia has not been clearly proposed. In simple linkage approaches, the results concerning the relationship between psychopathology and QoL have been inconsistent (Galletly et al., 1999; Ho et al., 1998; Carpinello et al., 1997; Packer et al., 1997; Patterson et al., 1997; Larsen and Gerlach, 1996), while Thomas et al. (1999) have found stronger association between negative symptoms and QoL in stable schizophrenia compared with acute exacerbation. The inconsistencies of the results partly seemed to depend on the study design used, as studies have often reported a lack of association between clinician-rated psychopathology and patient-reported QoL (e.g., Carpinello et al., 1997; Larsen and Gerlach, 1996). Reports concerning the relationship between QoL and neurocognitive function in chronic patients of schizophrenia were also inconsistent (Ritsner, 2007; Fujii et al., 2004; Buchanan et al., 1998; Heslegrave et al., 1997), which were true also for those on the relationship with executive function (Fiszdon et al., 2008; Greenwood et al., 2008; Matsui et al., 2008; Tyson et al., 2008; Weickert et al., 2000). On the other hand, better insight and presence of side effects have been consistently cited to be associated with poorer evaluation of QoL due to depression and physical discomfort (Karow et al., 2008; Yamauchi et al., 2008; Yen et al., 2008; Kongsakon et al., 2006; Hofer et al., 2004; Awad et al., 1997). Over time, however, as in chronic patients, presence of intact insight may contribute to better management of their symptoms and adherence to treatment, whereby resulting in improved QoL (Roseman et al., 2008). Furthermore, as decreased psychopathology is associated with both improved insight and better QoL, there is a strong possibility that insight may moderate between psychopathology and QoL. As for side effects, there is a lack of studies that consider the mediating effect of side effects between psychopathology and QoL. For example, it is possible that certain symptoms domains, such as depression and anxiety, may contribute to negative evaluation of one's health, causing over-reporting of side-effects and worse QoL. Putzhammer et al. (2005) found subjective well-being to be predicted by either objectively measured side effects or psychopathology depending on the kind of antipsychotic treatment, but like many studies that did not consider the implication of psychopathology on both side effects and QoL, they also did not examine the possible relationship between the two predictors of QoL. On the other, however, in chronic patients, side-effects, especially those that are self-reported, may be more strongly associated with executive function, as Hill et al. (2008) have reported significant relationships between physiological symptoms and cognitive functioning, but Bender et al. (2006) have found improvement in executive function to be unrelated to easing of extrapyramidal side effects.

The relationships between the predictors and QoL found in previous studies may have been at least partly clouded by insufficiently accounting for the dynamics among the predictors. As the above discussion illustrates, a number of hypotheses concerning the linkages

between the predictors in relation to QoL may be formulated, but simple linkage approaches, such as correlations and regressions, may not be sufficient for testing a number of inter-related questions simultaneously. For example, how much does psychopathology predict insight and cognitive impairment, and how are they, in turn, related to each other and to QoL? Can side effects be considered independent from other variables in predicting QoL? By considering these questions simultaneously, we can begin to understand the processes through which QoL may be determined.

The utility of the structural equation modelling (SEM) method in delineating multi-level relationships among the predictors of QoL in different clinical populations has been proven in previous studies (e.g., Urbanoski et al., 2007; Van De Ven et al., 2007), and we applied the SEM to simultaneously test a number of possible hypotheses concerning the inter-relations among the predictors of QoL in schizophrenia patients. In doing so, we applied clinician-rated measures for both psychopathology and QoL, as studies have often reported incongruous results by applying different modes of assessment for psychopathology and subjective QoL. The hypotheses we aimed to examine were the presence of mediating or moderating roles of insight, executive function, and self-reported side-effects between psychopathology and QoL and of linkages among these mediating variables in chronic patients of schizophrenia.

2. Methods

2.1. Subjects

A total of 72 patients (male = 23, female = 49) of chronic schizophrenia with the mean age of 39.3 ± 10.7 years receiving community based mental health services at two Community Mental Health Centers in the Seoul Metropolitan District and one Community Mental Health Center in the Incheon Metropolitan City were recruited. These patients were managed and regularly followed by mental health case-managers. All written informed consent forms were obtained from the participants prior to initiating any study procedures.

2.2. Measures

2.2.1. Psychopathology

The 18-item Brief Psychiatric Rating Scale (BPRS; Overall, 1976, 1983) was used to measure overall psychopathology of the patients. The BPRS not only measures the severity of psychotic symptoms, it also includes affective components such as tension, anxiety, and depressive mood. It is rated based on 7-point Likert scale, ranging from 1 (not present) to 7 (extremely severe).

2.2.2. Quality of life

The Korean standardized version of the Heinrichs Quality of Life Scale (QLS; Heinrichs et al., 1984; Song et al., 1999) was used to measure the functional aspects of daily life. This 21-item scale is objectively rated based on semi-structured interview with high end of the scale (scores of 5 or 6) reflecting normal or unimpaired functioning and the low end of the scales (scores of 0 or 1) reflecting severe impairment of function.

2.2.3. Insight

The standardized Korean version of the 9-item abridged Scale to Assess Unawareness of Mental Disorder (SUMD-K; Amador et al., 1994; Song et al., 2006) was used to measure the level of insight in patients. The score of 1 indicated presence of insight for the given symptom, while 3 indicated severe lack of insight. However, since the scale was designed to assess the insight of only the symptoms that are present, such as hallucination and blunted affect, the total score divided by the number of symptoms present was used as the index of the lack of insight.

Table 1Demographic description of the patients ($n=72$).

Female(%)	49(68.1)
Age (yr.)	39.33 $\pm$ 10.66
Age of onset (yr.)	24.39 $\pm$ 9.36
Duration of illness (yr.)	14.99 $\pm$ 8.78
Years of education (yr.)	10.46 $\pm$ 3.83
Marriage status (%)	Married(15.3), widowed(5.6), separated(4.2), divorced(5.6), single(68.1)
Living arrangement (%)	Living with family(68.1), living alone(13.9)
Physical illness (%)	Illness present(32.4)
Antipsychotic medication (%)	Presently on medication (95.8)
Disability status (%)	Registered as disabled(72.2)

2.2.4. Executive function

The Executive Interview (EXIT) developed by Royall et al. (1992) to measure general executive function was administered by either trained psychiatric nurses or mental health case-managers. It contains 25 items and requires 10 min to administer, and possible score ranges from 0 to 50 with higher scores indicating more severe impairment in executive function.

2.2.5. Side effects

The Korean version of Liverpool University Neuroleptic Side Effects Scale (LUNSERS) was used to obtain patient-reported side effects (Day et al., 1995; Jung et al., 2002). Presented in a 5-point Likert scale format from 0 (None) to 5 (Very Severe), the LUNSERS contains 41 items that can be considered symptoms due to neuroleptics side effects and 10 red herring items purported to be unrelated to neuroleptic effects. Here, we used the LUNSERS total score to reflect the total subjective discomfort felt by the patients.

2.3. Data analysis

For the purpose of constructing a set of viable models for SEM, we considered three possible conceptual relationships among the predictors of QoL based on above discussion. First, as one-level linkage studies have suggested, psychopathology, insight, executive functioning may be inter-correlated and may each partly predict QoL, with side-effects also predicting QoL, albeit independently. Second, the effect of psychopathology on QoL may be mediated by either insight or executive function, or both. Third, impairment in executive function may affect insight or self-reported side effects, which in turn may result in negative evaluation of QoL. Through these considerations, we formulated four hypothetical SEM models which could be compared for their relative fitness. The first model designated psychopathology, insight, executive functioning, and side-effects as primary predictors of QoL with inter-correlations among psychopathology, insight, and executive function. The second model designated insight and executive function as the mediators between psychopathology and QoL, with side-effects as an independent predictor of QoL. The third model was identical to the second model, except that executive function now also predicted self-reported side-effects. The fourth hypothetical model was also identical to the second model, except that both executive function and insight predicted self-reported side-effects.

The SEM models based on the above were constructed and examined for their fitness. The variables were connected by either unidirectional arrows signifying predictability (i.e., regression) or bi-directional arrows signifying association (i.e., correlation). Hence, in the first model, for example, the BPRS, SUMD, EXIT were inter-connected with bi-directional arrows and each had a unidirectional arrow drawn to QLS as did the LUNSERS, which was not connected to any other variables. In the second model, unidirectional arrows were drawn from the BPRS to the EXIT, SUMD, and QLS, while the EXIT and SUMD also each had a unidirectional arrow drawn to QLS. In addition, the LUNSERS was also connected to the QLS by a unidirectional arrow. Similar processes were carried out for the third and the fourth models. Lastly, the mediating or

moderating effects of EXIT, SUMD, and LUNSERS were tested by excluding the given variable from the respective models and then examining the changes in both the amount of total variance of QLS explained and regression coefficients in the adjusted models.

For the analysis and comparison of the relative fitness of the above models, Amos 5.0 (Amos Development Corporation, Spring House, Pennsylvania, USA) was used. The indices of goodness-of-fitness we have included were non-significant χ^2 statistic (i.e., probability value of less than .05 results in rejection of the model), adjusted goodness of fit index (AGFI: This index takes into account the degree of freedom available for testing the model), comparative fit index (CFI: This index is insensitive to sample size), Tucker–Lewis Index (TLI), and the root mean square error of approximation (RMSEA). The values close to 1, or above .95 indicate good fitness for AGFI, GFI, and TLI, while RMSEA values below .06 is required for the model to be considered fit (Hu and Bentler, 1999; Bentler, 1990). The lower(LO) and upper(HI) boundaries of a two-sided 90% confidence interval for the population RMSEA were also included.

All other statistical analyses were carried out with SPSS 13.0 (SPSS Inc., Chicago, Illinois, USA) by applying significance level of $p<0.05$ to all analyses.

3. Results

3.1. Demographic variables

Table 1 presents the demographic and clinical descriptions of our patients. There were no significant differences between male and female patients in age, age of onset, duration of illness, and years of education.

3.2. Clinical variables

Presented on the Table 2 are the means and SDs of the clinical variables. The data for the LUNSERS was obtained from a total of 61 patients because 11 patients did not complete the LUNSERS due to refusal or incapability. Further analysis revealed that there was no significant difference between the completers and non-completers in terms of BPRS total scores and its subscales, as well as in the total scores of the EXIT, SUMD, and QLS.

3.3. Model derivation and validation

The models have been constructed as described above and were examined for their fitness. The first model, which assumed presence of no mediating effects of any variables, satisfied the non-significant χ^2 test, but did not satisfy other indices of fitness ($\chi^2=5.573$, $df=3$, $P=0.134$; CFI = .923; TLI = .614; RMSEA = 0.110, LO = 0.000, HI = 0.251). The second model, which assumed the mediating effects of the executive function and insight between psychopathology and quality of life, also did not satisfy the required level of goodness of fit ($\chi^2=5.600$, $df=4$, $P=0.231$; CFI = .952; TLI = .820; RMSEA = 0.075, LO = 0.000, HI = 0.206). However, through this model, the standardized regression coefficient from the BPRS to SUMD was found to be .51, explaining 26% of variance, while that from the BPRS to EXIT was merely

Table 2Mean scores and SDs of clinical variables ($n=72$).

	Mean	SD
BPRS	41.57	12.50
EXIT	14.43	5.06
LUNSERS ¹	91.57	33.98
SUMD total score	9.51	6.00
No. response items	5.18	2.16
Total score/response items	1.73	.62
QLS	60.50	26.10

¹Based on 61 patients. BPRS = Brief Psychiatric Rating Scale, EXIT = Executive Interview, LUNSERS = Liverpool University Neuroleptic Side Effects Rating Scale, SUMD = Scale to Assess Unawareness of Mental Disorder, QLS = Korean Heinrichs Quality of Life Scale.

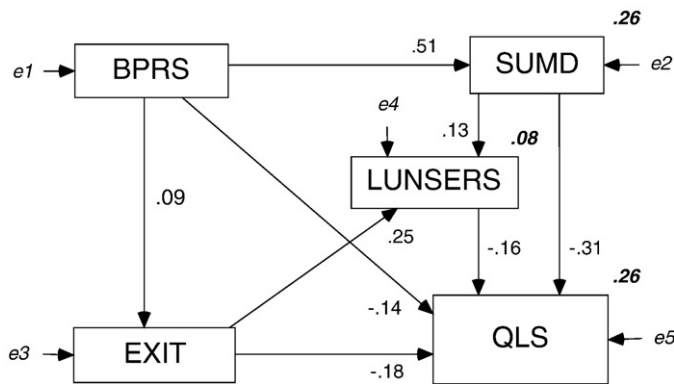


Fig. 1. The causal model of quality of life in chronic patients of schizophrenia. The figures associated with unidirectional arrows signify standardized regression coefficients, while bold italicized figures at the corners of SUMD, LUNERS, EXIT and QLS denote R^2 values. 'e' signifies error variance. BPRS = Brief Psychotic Rating Scale, SUMD = Scale for Unawareness of Mental Disease, LUNERS = Liverpool University Neuroleptic Side Effects Scale, EXIT = Executive Interview, QLS = Korean Heinrichs Quality of Life Scale.

.09, explaining 1% of variance. Hence, it was deduced that only the SUMD is likely to mediate between BPRS and QLS. The third model, where the LUNERS was designated as the mediator between EXIT and QLS, did satisfy all indices of goodness-of-fit ($\chi^2 = 1.578$, $df = 3$, $P = 0.664$; CFI = 1.000; TLI = 1.214; RMSEA = 0.000, LO = 0.000, HI = 0.156) explaining 24% of variance of QLS, and when the causal link between BPRS and EXIT was deleted from the model as suggested by the model 2, the adjusted model still retained its fitness ($\chi^2 = 2.106$, $df = 4$, $P = 0.716$; CFI = 1.000; TLI = 1.213; RMSEA = 0.000, LO = 0.000, HI = 0.132). The variance of the LUNERS explained by the EXIT was 6%. The fourth model, where LUNERS was designated as the mediator of EXIT and SUMD toward the QLS, was also found to have superior level of fitness ($\chi^2 = .386$, $df = 2$, $P = 0.825$; CFI = 1.000; TLI = 1.364; RMSEA = 0.000, LO = 0.000, HI = 0.139), explaining 26% of variance of QLS. The variance of LUNERS explained by EXIT and SUMD combined was 8%. Finally, when we removed the causal association between the BPRS and EXIT, the adjusted model also retained its superior level of fitness ($\chi^2 = .913$, $df = 3$, $P = 0.822$; CFI = 1.000; TLI = 1.313; RMSEA = 0.000, LO = 0.000, HI = 0.120), but the amount of variance of the QLS explained decreased by 1%. Fig. 1 provides an illustration of the final model (model 4) of complex causal relationships among the predictor of QLS. However, for the purpose of predicting the level QLS with these variables, the adjusted model that excludes the causal link between the BPRS and EXIT may be considered more parsimonious.

The analysis of mediation effects was carried out based on the fourth model. When SUMD was removed from the model, the total variance of QLS explained dropped to 18% and the standardized coefficients of BPRS and the LUNERS increased to $-.30$ and $-.20$, respectively. On the other hand, when the EXIT was removed from the model, the total variance of QLS decreased somewhat to 23%, and the standardized coefficients of BPRS and the LUNERS increased to $-.16$ and $-.21$, respectively. Hence, such results supported the partial mediating effect of insight, but not executive function, between psychopathology and quality of life in chronic patients of schizophrenia. Lastly, when the LUNERS was removed from the model, the standardized regression coefficients of SUMD and EXIT increased to $-.34$ and $-.22$, respectively, but that of BPRS decreased minimally to $-.13$. In addition, the variance of QLS explained decreased to 23%. Hence, these results suggested that side effects are likely to be a partial mediator for executive function and insight in determining the level of quality of life.

4. Discussion

Our study illustrates in part the complexity of the relationships among the predictors of QoL in chronic patients of schizophrenia,

which should be considered when designing research for this group. As our model demonstrates, the severity of psychopathology not only directly causes poor QoL, but also by adversely affecting insight. On the other hand, executive function may not be affected significantly by psychopathology, but it still plays an important role in determining the QoL not only directly, but also indirectly by influencing self-evaluation of side-effects. In summary, impaired insight and executive function caused by severe level of psychopathology contribute to an increased reporting of side-effects, resulting in cumulative dysfunction in daily life for patients with chronic schizophrenia.

Our model is mostly consistent with the causal links found in previous studies, but it has some important implications for the interpretation of their results on QoL of chronic patients of schizophrenia. For example, studies (e.g., Rocca et al., in press; Karow et al., 2005; Hofer et al., 2004) that have examined the effect of psychopathology on QoL without considering the mediating effect of insight may have reported somewhat inflated effect. This is especially true, since those studies have cited depressive symptoms, which have been found to be significantly linked with insight (Lincoln et al., 2007; Drake et al., 2004; Smith et al., 1998), as one of the significant predictors of QoL. Another example may be types of research that evaluates safety of drugs or QoL through self-reported side effects without considering the cognitive functions of patients. According to our study, more severe impairment in executive function leads to increased reporting of side-effects, and this effect is relatively independent from the severity of psychopathology. Hence, for such studies, objective measures should be complementarily used with the subjective reports or neurocognitive tests should be applied for more accurate evaluation of side effects and QoL.

According to our model, more severe lack of insight causes increased reporting of side effects, and this led to yet another hypothesis that psychopathology may also affect self-reporting of side effects. Hence, we conducted additional *post hoc* analysis by designating BPRS as a predictor of the LUNERS and comparing the models that either included or excluded the SUMD. As the result, when the SUMD was included, the model proved to have a good fit ($\chi^2 = .913$, $df = 3$, $P = 0.822$; CFI = 1.000; TLI = 1.313; RMSEA = 0.000, LO = 0.000, HI = 0.120) and the standardized regression coefficient of BPRS toward the LUNERS was found to be $-.10$. However, with the removal of the SUMD, the model still retained its fitness ($\chi^2 = .555$, $df = 2$, $P = 0.758$; CFI = 1.000; TLI = 1.326; RMSEA = 0.000, LO = 0.000, HI = 0.160) while the standardized regression coefficient of BPRS it changed to $.02$ and the total explained variance of the LUNERS also dropped from 9% to 6%. Such results therefore suggested the possible moderating role of insight between psychopathology and side effects, i.e. chronic patients with more severe level of psychopathology may be less likely to report side-effects once we control for their lack of insight. This hypothesis however has not been tested by previous reports to the best of our knowledge, and it warrants further confirmation by future studies.

Another linkage of interest was that between executive function and insight, but the amount of variance explained in the SUMD did not increase at all with the addition of the causal link from the EXIT, whose standardized coefficient toward the SUMD was merely $.02$. Hence, it can be concluded that little or no association exists between insight and executive function, as measured by the EXIT, in patients with chronic schizophrenia. Similar results of little or no association between executive function and insight have been obtained by a number of studies (Simon et al., 2009; Arduini et al., 2003; Young et al., 1998; Cuesta et al., 1995), but they mostly relied on the use of WCST, which has been found to be significantly associated with insight in other studies (Lysaker et al., 2003a,b; Laroi et al., 2000; Marks et al., 2000). As the original authors of the EXIT have found it to be moderately correlated with WCST (Royall et al., 1992), there is a likely possibility that the shared components of executive functions measured by both tests may not be able to reflect the cognitive ability associated with insight. This may be true especially when the association between executive function and insight is not specific, as

suggested by Donohoe et al. (2005). Hence, the lack of relationship between the executive function and insight in chronic patients proposed by our model needs to be confirmed with other measures of executive functions in future.

While our model included some of the major predictors of QoL, they were by no means intended to be exhaustive. In fact, the amount of total variance explained by the four major predictors was disappointingly small, owing to their shared effects. Some of the possible variables that should be considered in addition to our model include therapeutic alliance, attitude toward medication, and personality factors. Also, further extension of our model can be achieved by incorporating a broader range of neurocognitive functions and including subjective measures of QoL, which may explain some of the discrepancies found between the studies of QoL of chronic schizophrenia using different measures (e.g., Fitzgerald et al., 2003; Ruggeri et al., 2001; Atkinson et al., 1997). However, the use of self-reported QoL may not yield similar results, since it may be subject to distinct clinical variables, such as depressive symptoms, while objective QoL may be more influenced by negative symptoms or psychosocial performance (Aki et al., 2008; Kusel et al., 2007; Fitzgerald et al., 2001; Atkinson et al., 1997; Carpiello et al., 1997). As such, the QLS used in our study as an objective measure of QoL was likely to have been subjected to the influence of especially the negative symptoms. Our post hoc correlation analysis of the negative symptoms of the BPRS (i.e., a composite score of withdrawal, retardation, and blunted affect items) with QLS did reveal a significant correlation between the two measures ($r = -.35, p < .01$), hence future studies with a larger sample of chronic patients may focus on expanding the model by considering the differential effects of positive and negative symptoms on the QoL and its predictors. Meanwhile, Kusel et al. (2007) have found a significant moderate relationship between the objective and subjective measures of QoL, and studies by Wehmeier et al. (2007a,b) also have provided evidences that correspondence between the subjective measure, i.e., the Subjective Well-being on Neuroleptics, and QLS emerges and increases when the patients are examined longitudinally. As they have identified sex, age and severity of psychopathology as the predictors of concordance between the measures, future studies to confirm and expand our model using a subjective measure of QoL should first consider controlling these variables and also using longitudinal design. Otherwise, unsystematic inclusion of the above variables without a careful consideration and review of the past findings would likely require unnecessarily large sample and produce results that are prone to misinterpretations.

5. Conclusion

Our study illustrated the complexity of the interaction between the predictors of QoL in chronic schizophrenia. It is unclear whether such model can be also extended to acute stage and further research is necessary to confirm the mediating roles of insight, executive function, and side effects in acute exacerbation. Nonetheless, the approach used in this study may yield more consistent results for specific target patient groups in the long run, which will invariably lead to more effective strategies to improve their quality of life.

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References

- Aki H, Tomotake M, Kaneda Y, Iga J, Kinouchi S, Shibuya-Tayoshi S, et al. Subjective and objective quality of life, levels of life skills, and their clinical determinants in outpatients with schizophrenia. *Psychiatry Res* 2008;158:19–25.
- Amador XF, Flaum M, Andreasen NC, Strauss DH, Yale SA, Clark SC, et al. Awareness of illness in schizophrenia, schizoaffective and mood disorders. *Arch Gen Psychiatry* 1994;51:826–36.
- Arduini L, Kalyvoka A, Stratta P, Rinaldi O, Daneluzzo E, Rossi A. Insight and neuro-psychological function in patients with schizophrenia and bipolar disorder with psychotic features. *Can J Psychiatry* 2003;48:338–41.
- Atkinson M, Sharon Z, Chuang H. Characterizing quality of life among patients with chronic mental illness: a critical examination of the self-report methodology. *Am J Psychiatry* 1997;154:99–105.
- Awad AG, Voruganti LN, Heslegrave RJ. A conceptual model of quality of life in schizophrenia: description and preliminary clinical validation. *Qual Life Res* 1997;6:21–6.
- Bender S, Dittmann-Balcar A, Schall U, Wolstein J, Klimke A, Riedel M, et al. Influence of atypical neuroleptics on executive functioning in patients with schizophrenia: a randomized, double-blind comparison of olanzapine vs. clozapine. *Int J Neuropsychopharmacol* 2006;9:135–45.
- Bentler PM. Comparative fit indices in structural models. *Psychol Bull* 1990;107:238–46.
- Browne S, Roe M, Lane A, Gervin M, Morris M, Kinsella A, et al. Quality of life in schizophrenia: relationship to sociodemographic factors, symptomatology and tardive dyskinesia. *Acta Psychiatr Scand* 1996;94:118–24.
- Buchanan RE, Breier A, Kirkpatrick B, Ball P, William T, Carpenter J. Positive and negative symptom response to clozapine in schizophrenic patients with and without the deficit syndrome. *Am J Psychiatry* 1998;155:751–60.
- Caldwell CB, Gottesman II. Schizophrenics kill themselves too: a review of risk factors for suicide. *Schizophr Bull* 1990;16:571–89.
- Caldwell CB, Gottesman II. Schizophrenia — a high risk factor for suicide: clues to risk reduction. *Suicide Life Threat Behav* 1992;22:479–93.
- Carpiello B, Lai GL, Pariente CM, Carta MG, Rudas H. Symptoms, standards of living and subjective quality of life: a comparative study of schizophrenia and depressed outpatients. *Acta Psychiatr Scand* 1997;96:235–41.
- Cuesta MJ, Peralta V, Caro F, de Leon J. Is poor insight in psychotic disorders associated with poor performance on the Wisconsin Card Sorting Test? *Am J Psychiatry* 1995;152:1380–2. Erratum in *Am J Psychiatry*. 1996;153:270.
- Day JC, Wood G, Dewey M, Bentall R. A self-rating scale for measuring neuroleptic side effects. Validation in a group of schizophrenic patients. *Br J Psychiatry* 1995;166:650–3.
- Dickerson FB, Ringel NB, Parente F. Subjective quality of life in out-patients with schizophrenia: clinical and utilization correlates. *Acta Psychiatr Scand* 1998;98:124–7.
- Donohoe G, Corvin A, Robertson IH. Are the cognitive deficits associated with impaired insight in schizophrenia specific to executive task performance? *J Nerv Ment Dis* 2005;193:803–8.
- Drake RJ, Pickles A, Bentall RP, Kinderman P, Haddock G, Tarrierand N, et al. The evolution of insight, paranoia and depression during early schizophrenia. *Psychol Med* 2004;34:285–92.
- Eack SM, Newhill CE. Psychiatric symptoms and quality of life in schizophrenia: a meta-analysis. *Schizophr Bull* 2007;33:1225–37.
- Fiszdon JM, Choi J, Goulet J, Bell MD. Temporal relationship between change in cognition and change in functioning in schizophrenia. *Schizophr Res* 2008;105:105–13.
- Fitzgerald PB, de Castella AR, Filia K, Collins J, Brewer K, Williams CL, et al. A longitudinal study of patient- and observer-rated quality of life in schizophrenia. *Psychiatry Res* 2003;119:55–62.
- Fitzgerald PB, Williams CL, Corteling N, Filia SL, Brewer K, Adams A, et al. Subject and observer-rated quality of life in schizophrenia. *Acta Psychiatr Scand* 2001;103:387–92.
- Fujii DE, Wylie AM, Nathan JH. Neurocognition and long-term prediction of quality of life in outpatients with severe and persistent mental illness. *Schizophr Res* 2004;69:67–73.
- Galletly CA, Clark CR, McFarlane AC, Weber SL. Effects of clozapine for non-treatment resistant patients with schizophrenia. *Psychiatr Serv* 1999;50:101–3.
- Greenwood KE, Morris R, Sigmundsson T, Landau S, Wykes T. Executive functioning in schizophrenia and the relationship with symptom profile and chronicity. *J Int Neuropsychol Soc* 2008;14:782–92.
- Heinrichs DW, Hanlon TE, Carpenter Jr WT. The Quality of Life Scale: an instrument for rating the schizophrenia syndrome. *Schizophr Bull* 1984;10:388–98.
- Heslegrave RJ, Awad AG, Voruganti LN. The influence of neurocognitive deficits and symptoms on quality of life in schizophrenia. *J Psychiatry Neurosci* 1997;22:235–43.
- Hill SK, Reilly JL, Harris MSH, Khine T, Sweeney JA. Oculomotor and neuropsychological effects of antipsychotic treatment for schizophrenia. *Schizophr Bull* 2004;34:494–506.
- Ho BC, Nopoulos P, Flaum M, Arud S, Andreasen NC. Two year outcome in first episode schizophrenia: predictive value of symptoms for quality of life. *Am J Psychiatry* 1998;155:1196–201.
- Hofer A, Kemmler G, Eder U, Edlinger M, Hummer M, Fleischhacker WW. Quality of life in schizophrenia: the impact of psychopathology, attitude toward medication, and side effects. *J Clin Psychiatry* 2004;65:932–9.
- Hu L, Bentler PM. Cutoff criteria for fit indexes in covariance structure analysis: conventional criteria versus new alternatives. *Struct Equ Modeling* 1999;6:1–55.
- Jung HY, Joo YH, Shin HK, Chung EK, Kang UG, Roh MS, et al. A validation study of Korean-version of Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS). *J Korean Neuropsychiatr Assoc* 2002;41:138–45.
- Karow A, Pajonk FG, Reimer J, Hirdes F, Osterwald C, Naber D, et al. The dilemma of insight into illness in schizophrenia: self- and expert-rated insight and quality of life. *Eur Arch Psychiatry Clin Neurosci* 2008;258:152–9.
- Karow A, Moritz S, Lambert M, Schoder S, Krausz M. PANSS syndromes and quality of life in schizophrenia. *Psychopathology* 2005;38:320–6.
- Kongsakon R, Trinidad-Oñate P, Chaudhry HR, Raza SB, Leynes CR, Khan IU, et al. Asian outpatients with schizophrenia: a double-blind randomized comparison of quality of life and clinical outcomes for patients treated with olanzapine or haloperidol. *J Med Assoc Thai* 2006;89:1157–70.
- Kusel Y, Laugharne R, Perrington S, McKendrick J, Stephenson D, Stockton-Henderson J, et al. Measurement of quality of life in schizophrenia: a comparison of two scales. *Soc Psychiatry Psychiatr Epidemiol* 2007;42:819–23.
- Landmark J, Cernovsky ZZ, Merskey. Correlates of suicide attempts and ideation in schizophrenia. *Br J Psychiatry* 1987;151:18–20.

- Larøi F, Fannemel M, Ronneberg U, Flekkoy K, Opjordsmoen S, Dullerud R, et al. Unawareness of illness in chronic schizophrenia and its relationship to structural brain measures and neuropsychological tests. *Psychiatry Res* 2000;100:49–58.
- Larsen EB, Gerlach J. Subjective experience of treatment, side effects, mental state and quality of life in chronic schizophrenic out patients treated with depot neuroleptics. *Acta Psychiatr Scand* 1996;93:381–8.
- Lincoln TM, Lüllmann E, Rief W. Correlates and long-term consequences of poor insight in patients with schizophrenia. A systematic review. *Schizophr Bull* 2007;33:1324–42.
- Lysaker PH, Bryson GJ, Lancaster RS, Evans JD, Bell MD. Insight in schizophrenia: associations with executive function and coping style. *Schizophr Res* 2003a;59:41–7.
- Lysaker PH, Lancaster RS, Davis LW, Clements CA. Patterns of neurocognitive deficits and unawareness of illness in schizophrenia. *J Nerv Ment Dis* 2003b;191:38–44.
- Lysaker PH, Buck KD, Hammoud K, Taylor AC, Roe D. Associations of symptoms, psychosocial function and hope with qualities of self-experience in schizophrenia: comparisons of objective and subjective indicators of health. *Schizophr Res* 2006;82:241–9.
- Marks KA, Fastenau PS, Lysaker PH, Bond GR. Self-Appraisal of Illness Questionnaire (SAIQ): relationship to researcher-rated insight and neuropsychological function in schizophrenia. *Schizophr Res* 2000;45:203–11.
- Matsui M, Sumiyoshi T, Arai H, Higuchi Y, Kurachi M. Cognitive functioning related to quality of life in schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry* 2008;32:280–7.
- Melle I, Friis S, Haahr U, Johannesen JO, Larsen TK, Opjordsmoen S, et al. Measuring quality of life in first-episode psychosis. *Eur Psychiatry* 2005;20:474–83.
- Overall JE. The brief psychiatric rating scale. In: Rockville GW, editor. *ECDEU Assessment Manual*. National Institute of Mental Health; 1976.
- Overall JE. Brief psychiatric rating scale and brief psychiatric history form. In: Keller PA, Ritt LG, editors. *Innovations in Clinical Practice: A Source Book*. Sarasota FL: Professional Resource Exchange Inc; 1983. p. 307–16.
- Packer S, Husted J, Cohen S, Tomlinson G. Psychopathology and quality of life in schizophrenia. *J Psychiatr Neurosci* 1997;22:231–4.
- Patterson L, Shaw W, Semple SJ, Moscona S, Harris MJ, Kaplan RM, et al. Health-related quality of life in older patients with schizophrenia and other psychoses: relationships among psychosocial and psychiatric factors. *Int J Geriatr Psychiatry* 1997;12:452–61.
- Planasky K, Johnston R. The occurrence and characteristics of suicidal preoccupation and acts in schizophrenia. *Acta Psychiatr Scand* 1971;47:473–83.
- Pompili M, Amador XF, Girardi P, Harkavy-Friedman J, Harrow M, Kaplan K, et al. Suicide risk in schizophrenia: learning from the past to change the future. *Ann Gen Psychiatr* 2007;6:10.
- Ponizovsky AM, Grinshpoon A, Levav I, Ritsner MS. Life satisfaction and suicidal attempts among persons with schizophrenia. *Compr Psychiatry* 2003;44:442–7.
- Putzhammer A, Perfahl M, Pfeiff L, Hajak G. Correlation of subjective well-being in schizophrenic patients with gait parameters, expert-rated motor disturbances, and psychopathological status. *Pharmacopsychiatry* 2005;38:132–8.
- Ritsner MS. Predicting quality of life impairment in chronic schizophrenia from cognitive variables. *Qual Life Res* 2007;16:929–37.
- Rocca P, Giugiaro M, Montemagni C, Rigazzi C, Rocca G, Bogetto F. Quality of life and psychopathology during the course of schizophrenia. *Comp Psychiatry* in press. doi:10.1016/j.comppsy.2008.12.002.
- Roseman AS, Kasckow J, Fellows I, Osatuke K, Patterson TL, Mohamed S, et al. Insight, quality of life, and functional capacity in middle-aged and older adults with schizophrenia. *Int J Geriatr Psychiatry* 2008;23:760–5.
- Royall DR, Mahurin RK, Gray KF. Bedside assessment of executive cognitive impairment: the Executive Interview. *J Am Geriatr Soc* 1992;40:1221–6.
- Ruggeri M, Bisoffi G, Fontecedro L, Warner R. Subjective and objective dimensions of quality of life in psychiatric patients: a factor analytical approach: the South Verona Outcome Project 4. *Br J Psychiatry* 2001;178:268–75.
- Simon V, De Hert M, Wampers M, Peuskens J, van Winkel R. The relation between neurocognitive dysfunction and impaired insight in patients with schizophrenia. *Eur Psychiatry* 2009;24:239–43.
- Smith TE, Hull JW, Santos L. The relationship between symptoms and insight in schizophrenia: a longitudinal perspective. *Schizophr Res* 1998;33:63–7.
- Song W, Choi YH, Kim HS, Huh SY, Ko YT, Chang AK, et al. The Korean version of Heinrichs Quality of Life Scale (K-QOLS): a reliability and a validity study. *Korean J Psychopathol* 1999;8:86–97.
- Song J, Kim K, Lee S, Kim Y, Noh J, Kim J, et al. Reliability and validity of the Korean version of the Scale to Assessment Unawareness of Mental Disorder (SUMD-K). *J Korean Neuropsychiatr Assoc* 2006;45:307–15.
- Thomas CCB, Village DI, Miller A, Olsen J. Predicting quality of life from symptomatology in schizophrenia at exacerbation and stabilization. *Psychiatry Res* 1999;186:131–42.
- Tyson P, Laws K, Flowers K, Mortimer A, Schulz J. Attention and executive function in people with schizophrenia: relationship with social skills and quality of life. *Int J Psychiatr Clin Pract* 2008;12:112–9.
- Urbanoski KA, Cairney J, Adlaf E, Rush B. Substance abuse and quality of life among severely mentally ill consumers: a longitudinal modelling analysis. *Soc Psychiatry Psychiatr Epidemiol* 2007;42:810–8.
- Van De Ven MO, Engels RC, Sawyer SM, Otten R, Van Den Eijnden RJ. The role of coping strategies in quality of life of adolescents with asthma. *Qual Life Res* 2007;16:625–34.
- Weickert TW, Goldberg TE, Gold JM, Bigelow LB, Egan MF, Weinberger DR. Cognitive impairments in patients with schizophrenia displaying preserved and compromised intellect. *Arch Gen Psychiatry* 2000;57:907–13.
- Wehmeier PM, Kluge M, Schacht A, Helsing K, Schreiber W. Correlation of physician and patient rated quality of life during antipsychotic treatment in outpatients with schizophrenia. *Schizophr Res* 2007a;91:178–86.
- Wehmeier PM, Kluge M, Schneider E, Schacht A, Wagner T, Schreiber W. Quality of life and subjective well-being during treatment with antipsychotics in out-patients with schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry* 2007b;31:703–12.
- Whitty P, Browne S, Clarke M, McTigue O, Waddington J, Kinsella T, et al. Systematic comparison of subjective and objective measures of quality of life at 4-year follow-up subsequent to a first episode of psychosis. *J Nerv Ment Dis* 2004;192:805–9.
- Yamauchi K, Aki H, Tomotake M, Iga J, Numata S, Motoki I, et al. Predictors of subjective and objective quality of life in outpatients with schizophrenia. *Psychiatry Clin Neurosci* 2008;62:404–11.
- Yen CF, Cheng CP, Huang CF, Yen JY, Ko CH, Chen CS. Quality of life and its association with insight, adverse effects of medication and use of atypical antipsychotics in patients with bipolar disorder and schizophrenia in remission. *Bipolar Disord* 2008;10:617–24.
- Young DA, Zakzanis KK, Bailey C, Davila R, Griesse J, Sartory G, et al. Further parameters of insight and neuropsychological deficit in schizophrenia and other chronic mental disease. *J Nerv Ment Dis* 1998;186:44–50.