Quality of life in stable schizophrenia: The relative contributions of disorganization and cognitive dysfunction.

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Abstract

Objective

The purpose of this study was to examine the relative contributions of disorganization and cognitive dysfunction to quality of life (QOL) in patients with stable schizophrenia.

Methods

A total of 276 consecutive outpatients with stable schizophrenia were enrolled in a cross-sectional study. We performed a mediation analysis to assess the specific effect of disorganization on QOL, as assessed by the Heinrichs–Carpenter Quality of Life Scale (QLS), and the possible mediating role of cognitive dysfunction.

Results

Our findings were as follows: (i) disorganization was negatively related to the total QLS score; (ii) disorganization was negatively related to two of the four QLS domains, namely the role-functioning domain (occupational/educational) and the intrapsychic functioning domain (e.g., motivation, curiosity, and empathy); and (iii) verbal memory was a partial mediator of the relationship between disorganization and QLS (the total score and the two above-mentioned domains).

Conclusions

Disorganization demonstrated direct and indirect effects via verbal memory on two domains of functioning, as measured by the QLS. These results highlight the importance of improving disorganization and cognition (particularly verbal memory) to improve the functional outcomes of patients with schizophrenia.

Keywords

Schizophrenia; Quality of life; Disorganization; Cognitive dysfunction; Mediation analysis

1. Introduction

Regarding the factors that influence quality of life (QOL) in patients with schizophrenia, the majority of researchers have primarily focused on psychiatric symptoms, although many other influential predictors have been identified (Eack et al., 2007). Indeed, one factor that has been shown to be consistently

negatively associated with QOL is psychopathology (Lambert and Naber, 2004). QOL has been negatively correlated with positive, negative, and general psychopathology, as well as with depressive symptoms; some studies have found a large relationship between these measures (Norman et al., 2000, Fitzgerald et al., 2001 and Rocca et al., 2005), while other studies have identified only a small to moderate relationship (Sim et al., 2004 and Ritsner et al., 2005). In many of these studies, positive symptoms, such as hallucinations and delusions, were combined with conceptual disorganization to form a positive symptom factor. Over time, several factor-analytic studies (Norman et al., 1997 and Meagher et al., 2000) have supported the view that delusions and hallucinations are distinct from positive symptoms, such as formal thought disorders. As a result, disorganization has emerged as a separate domain worthy of consideration. Disorganization was introduced by Liddle (1987) as an important third factor in addition to the positive and negative symptom factors. According to Liddle, schizophrenic symptoms segregated into three syndromes: psychomotor poverty (poverty of speech, lack of spontaneous movement and various aspects of blunting of affect); disorganization (inappropriate affect, poverty of content of speech, and disturbances of the form of thought); and reality distortion (particular types of delusions and hallucinations). Some studies have suggested that disorganization may be a stronger predictor of community function than reality distortion (Norman et al., 1999 and Ventura et al., 2009).

Much more attention has been paid to cognitive dysfunction because it may lead to poor community functioning, including social functioning, work performance, and social skills (Bryson and Bell, 2003). Cognitive deficits persist throughout the illness and serve as rate-limiting factors associated with functional recovery (Keefe and Fenton, 2007). Studies investigating the ability of neurocognitive variables to predict QOL in individuals with schizophrenia have yielded conflicting results. However, a recent meta-analysis revealed a markedly different relationship between neurocognition and objective and subjective QOL (Tolman and Kurtz, 2012). Small to moderate relationships ($d \leq 0.55$) were found between crystallized verbal ability, working memory verbal list learning, processing speed, and the executive function and objective indices associated with QOL. In contrast, the results revealed either nonsignificant or inverse relationships for the vast majority of neurocognitive measures and measures of subjective QOL.

Concerning the relationships between cognition and symptoms, there is evidence in the literature of strong correlations between performance on neurocognitive tests and negative symptoms (Ventura et al., 2009). Differential relationships between positive symptoms and neurocognitive functioning have been reported. Symptoms of disorganization, when reported as a factor separate from reality distortion, appear to be related to neurocognition and warrant a separate empirical study. A recent meta-analysis demonstrated a small to moderate ($r = -0.23$) relationship between disorganization and neurocognition, while the relationship between neurocognition and reality distortion was relatively weak ($r = -0.04$). Disorganization was related to all of the domains of cognitive functioning examined, including verbal memory ($r = -0.20$), attention/vigilance ($r = -0.25$), reasoning and problem solving ($r = -0.24$), processing speed ($r = -0.26$), visual memory ($r = -0.20$), and working memory ($r = -0.20$). In contrast, reality distortion showed no such broad association (r values ranging from −0.01 to −0.12) (Ventura et al., 2010).

Previous research has linked disorganization to neurocognition and neurocognition to QOL, although in separate studies. The present study was conducted to determine whether the relationship between disorganization and QOL may be mediated by the extent of cognitive deficits in patients with schizophrenia.

Thus, the objectives of the current study were three-fold. First, we investigated the ability of disorganization alone to predict QOL. Given the previous contradictory findings in the literature, we intended for this investigation to be an exploratory analysis and expected that the disorganization would

predict a significantly lower QOL. Second, we studied the ability of cognition alone to predict QOL. Given the results of previous studies, we anticipated a role for cognition in the prediction of QOL. Third, we explored the possibility that disorganization continues to predict QOL when cognition is also considered. It was expected that both disorganization and neuropsychological deficits interact to influence QOL, with neuropsychological deficits acting as partial mediators of the relationship between disorganization and QOL.

2. Materials and methods

2.1. Participants

This study was conducted at the Department of Neuroscience, Psychiatric Section, and the Department of Mental Health ASL TO1 Molinette-Turin, Italy. Between July 2008 and March 2010, we screened 345 schizophrenia spectrum patients of either gender, aged between 18 and 65 years. A total of 276 consecutive outpatients who met the inclusion criteria and agreed to participate in the study were enrolled. They all fulfilled the formal Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) (APA, 2000) diagnostic criteria for schizophrenia. This diagnosis was confirmed by two expert clinicians (C.M., M.S.) using the Structured Clinical Interview for DSM-IV (SCID) (First et al., 1997). Prior to this study, the interviewers received training sessions for the SCID. At the time of study entry, the patients had been clinically stable for at least 6 months, as judged by the treating psychiatrist. This result indicates that, during this period, all of the patients were treated as outpatients; their treatment regimens had not been modified; and there were no essential changes in their psychopathology. In addition to their medical records, all of the patients were considered to be in a stable state, as assessed from the reports of the patients themselves, as well as from the observations of the psychiatric staff, personnel in the psychiatric community, and relatives. Patients were evaluated using a semi-structured interview to assess their demographic and clinical features. Data were collected to determine age, gender, education, age at schizophrenia onset (report of first contact with a psychiatric service), and length of illness. Subjects were excluded if they had a current disorder other than schizophrenia on Axis I of the DSM-IV-TR (screened with the SCID), a current or past codiagnosis of autistic disorder or another pervasive developmental disorder, a history of severe head injury (coma ≥ 48 h), or a diagnosis of a psychiatric disorder due to a general medical condition. All of the patients were taking antipsychotic medication at the time of assessment. The two clinicians (C.M., M.S.) were aware of all previous diagnoses and were also able to review the previous clinical charts that were available for all patients.

Written informed consent was obtained from all subjects after a complete description of the study was provided. The study was carried out in accordance with the Declaration of Helsinki in 1995 (as revised in Edinburgh in 2000) and was approved by the Local Research Ethics Committee (LREC).

2.2. Psychiatric assessment

The overall illness severity was rated using the Clinical Global Impression-Severity Scale (Guy, 1976). Current levels of psychopathological symptoms were assessed using the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). Quality of life was evaluated using the Quality of Life Scale (QLS) (Heinrichs et al., 1984), which is a semistructured, clinician-rated interview that includes 21 items rated by the

clinician on 7-point scales in the following 4 domains: interpersonal relations and social network (IRSN), instrumental role functioning (IRF), intrapsychic foundations (IF), and common objects and activities (COA). The items were rated from 0 to 6, with higher scores reflecting a better QOL.

All assessments were performed by two expert clinicians (C.M., M.S.). In an attempt to reduce inter-rater variability, all raters were trained to administer the psychometric tests according to common standards. Raters also participated in a pilot study to reach a consensus on the ratings that were obtained using psychometric scales. The procedure for this pilot study involved the authors completing independent ratings of interviews that were conducted with 15 patients. This procedure was followed by a discussion about each patient until consensus ratings were reached. In this study, the agreement within one point between the raters varied from 79 to 91% of the time for all items on the PANSS, with variations in the total QLS score occurring 91% of the time. Efforts were made to maintain inter-rater reliability throughout the entire study period, including the performance of careful calibration and use of standardization procedures and regular, in-depth reviews of a sample of interviews with the lead author.

2.3. Cognitive assessment

Neuropsychological tests were administered by two trained psychologists (B.C.; F.C.) who were unaware of the patients' clinical characteristics or the results of their psychiatric rating scores. The test battery was administered and scored according to standard instructions in the same way for all subjects on the day after the psychiatric assessments. The total testing time ranged from 1 to 2 h per patient (one or two sessions). None of the subjects were familiar with the tests.

To evaluate the subjects' attentive functions, we used the Stroop Test (Stroop, 1935) and the Trail Making Test (TMT) (Reitan, 1958). For the purpose of our analysis, we used the number of colors named on a conflicting card (Stroop CW), which is an index of the sensitivity to interference and/or response inhibition, and the TMT b–a score, which is calculated as the difference between TMT-B and TMT-A times, to assess divided attention and set shifting.

Verbal memory was assessed using the California Verbal Learning Test (CVLT) (Delis et al., 1987) and, in particular, the total number of items correctly recalled over five learning trials (CVLT 1–5). To index the executive functions, we used the Wisconsin Card Sorting Test (WCST) (Heaton et al., 1993) and considered the number of achieved sorting categories (WCST cat), which is usually regarded as the main benchmark for the evaluation of the WCST.

2.4. Statistical analysis

We used a 5-factor model proposed by van der Gaag et al. (2006) to cover all 30 items of the PANSS. The five component factors are as follows: positive symptoms, negative symptoms, disorganization, excitement, and emotional distress. In this model, the disorganization factor was composed of stereotyped thinking, poor attention, disorientation, conceptual disorganization, difficulty in abstraction, mannerism, lack of judgment and insight, disturbance of volition, and preoccupation.

Data are presented as the means ± standard deviations (SD) or percentages (%) unless stated otherwise.

Analyses were planned in the following three stages. In stage 1, univariate linear regression analyses between the variables of interest (disorganization, neurocognition, total and domain-specific QLS scores) and between these variables and potential confounders (age, education, positive symptoms, negative symptoms, excitement, and emotional distress) were conducted. In stage 2, a series of multiple regression analyses using a backward elimination procedure was performed to determine the cross-sectional determinants of QLS scores. The first and second hypotheses were tested using total and domain-specific QLS scores as dependent variables and any significant variables in the initial univariate analyses ($p < 0.05$) as predictors. The predictors included patient age, education, and clinical (disorganization, positive symptoms, negative symptoms, excitement, emotional distress) and cognitive variables. Backward stepwise regression begins with a full or saturated (all regression terms included) model and variables are progressively removed from the equation in an iterative process, at consecutive steps, eliminating those that fail to meet the specified criterion (usually a parameter estimate p-value < 0.05). The fit of the model is tested after the elimination of each variable to ensure that the model still adequately fits the data. When no more variables can be eliminated from the model, the analysis has been completed. In stage 3, we performed mediational analyses using multiple regression analyses as specified by Baron and Kenny (1986). Mediation is said to occur when certain conditions are met, as follows: (1) the independent variable (IV) significantly predicts the dependent variable (DV) (path c or total effect); (2) the IV significantly predicts the potential mediator (M) (path a); (3) the M predicts the DV (path b); and (4) the effect of the IV on the DV is reduced when the M is included in the model (path c' or direct effect). Sobel tests for indirect effects were employed to determine whether this attenuation was significant and to determine whether M fully or partially mediated the relationship between the IV and the DV. We applied Sobel tests in order to decrease type I and type II error (Holmbeck, 1997).

Statistical analyses were performed using the Statistical Package for the Social Science, SPSS, version 17 for Windows (SPSS, Chicago, IL, USA). Sobel tests were computed with a SPSS macro developed by Preacher and Hayes (2004), into which certain statistics had to be entered as follows: (1) the unstandardized B coefficients for the relationships between the IV (the predictor) and the M; (2) the unstandardized B coefficients for the relationships between the IV and the DVs after controlling for the M; and (3) the standard errors of both unstandardized B coefficients. Sobel's significance test is both a test of the indirect effect of disorganization on the total QLS score, IRF, and IF (i.e., the product of the total disorganization → M and M → QLS scores, IRF, and IF pathways) and a test of a decrease in the total effect of disorganization on the total QLS score, IRF, or IF after accounting for the M (i.e., total effect–direct effect). In other words, the decrease in the total effect is mathematically equivalent to the magnitude of the indirect effect, as the total effect − direct effect = the indirect effect (MacKinnon and Dwyer, 1993).

3. Results

The patients in our study had DSM IV-TR schizophrenia diagnoses of the paranoid subtype (n = 158, 57%), disorganized subtype (n = 27, 10%), undifferentiated subtype (n = 57, 21%), or residual subtype (n = 34, 12%). The mean age (± S.D.) of our patients was 40 (± 10.8) years. The mean duration of illness (± S.D.) was 14.2 (± 9.74) years. There were 116 females (42%) and 160 males (58%). Sixty-two percent of patients were treated with second-generation antipsychotics (SGAs), and 38% were treated with first-generation antipsychotics (FGAs). Subjects showed a moderate severity of symptoms, as assessed by the PANSS and CGI-S. The mean (± S.D.) QOL rating in our sample, as assessed by the total QLS score, reflects intermediate

but quite significant levels of QOL impairment. The demographic and clinical features of our sample are presented in **Table 1**.

The results of the univariate linear regression analyses (Stage 1) are shown in **Table 2**.

Among the variables of interest that were significantly associated with QLS in the univariate analyses ($p < 0.05$) (Disorganization, Stroop CW; CVLT 1–5, TMT b–a), only two variables remained after backward selection (disorganization; CVLT 1–5) (Stage 2). All other variables were thus dropped from further mediational analyses.

To better understand the pattern of correlations among disorganization, CVLT 1–5 and QLS (total score, IRF, and IF), three mediational hypotheses were tested. The mediational models, with standardized βs, are presented in Fig. 1 and Fig. 2. In our case, the IV was disorganization; the hypothetical M was CVLT 1–5; and the outcome variables, the DVs, were the total QLS score, IRF, and IF. First, we tested the effect of disorganization on QLS total score, IRF and IF (**Fig. 1**). The effect of disorganization was significant, showing that higher disorganization symptoms predicted lower QLS total score ($\beta = -0.500$, S.E. = 0.173, $p < 0.001$; adjusted R2 = 0.303, accounting for 30.3% of the variance), IRF ($\beta = -0.425$, S.E. = 0.045, $p < 0.001$; adjusted R2 = 0.177, accounting for 17.7% of the variance), and IF ($\beta = -0.423$, S.E. = 0.067, $p < 0.001$; adjusted R2 = 0.208, accounting for 20.8% of the variance) (step 1 of Baron and Kenny method). Second, we inserted in the model CVLT 1–5 as potential M of the effects of disorganization (**Fig. 2**). As shown in **Fig. 2**, disorganization significantly predicted CVLT 1–5, with a higher severity of disorganization predicting lower CVLT 1–5 scores ($\beta = -0.529$, S.E. = 0.097, $p < 0.001$; adjusted R2 = 0.212, explaining 21.2% of the variance) (step 2 of Baron and Kenny method).

Third, CVLT 1–5 predicted QLS total score, with higher CVLT 1–5 predicting higher QLS ($\beta = 0.219$, S.E. = 0.101, $p < 0.001$), IRF ($\beta = 0.171$, S.E. = 0.033, $p = 0.004$), and IF ($\beta = 0.187$, S.E. = 0. 045, $p = 0.001$) scores (step 3 of Baron and Kenny method). Fourth, the direct coefficients (standardized Beta or β coefficients) of Disorganization on QLS total score, IRF, and IF remained significant after inclusion of CVLT 1–5 as mediating variable, while they decreased somewhat in magnitude (β from −0.500 to −0.471 for the total QLS score; β from −0.425 to −0.373 for the IRF; β from −0.423 to −0.368 for the IF) (step 4 of Baron and Kenny method). In our prediction models, the adjusted R2 value was 0.317 for the total QLS score model, accounting for 31.7% of the variance. In the IRF model, the adjusted R2 value was 0.181, accounting for 18.1% of the variance. Finally, in the IF model, the adjusted R2 value was 0.207, accounting for 20.7% of the variance.

However, the reduction of the direct effect of disorganization on QLS total score ($z = 3.91$, $p < 0.001$), on IRF ($z = 6.02$, $p < 0.001$), and on IF ($z = 2.93$, $p = 0.003$) was significant, providing further support for the hypothesis that CVLT 1–5 acts as a partial mediator between disorganization and the total QLS total score, IF, and IRF. Thus, it appears that CVLT 1–5 acts as a partial M and does not completely mediate the relationship between disorganization and the total QLS score, IRF, and IF. However, our results would suggest that the indirect relationship between disorganization and QLS total core, IF, and IRF, as mediated by CVLT 1–5, is weak but non-negligible.

4. Discussion

The purpose of the present study was to examine the interactions between disorganization and cognition in predicting QOL within a sample of outpatients with stable schizophrenia.

First, as hypothesized, disorganization was negatively related to QOL. In the literature, there is evidence that disorganization is the most reliable predictor of a variety of outcome indicators (Heslegrave et al., 1997, Norman et al., 1999, Smith et al., 1999 and Ventura et al., 2009). Recently, Ventura et al. (2010) hypothesized that the close link between disorganization and outcome indicators may be due to the interference of disorganization symptoms on functional aspects of communication and social interactions, as well as to the lack of compensatory mechanisms. The strong, statistically significant correlation between disorganization and QOL in our study supports the necessity of dealing with disorganization as a separate positive symptom factor.

Another interesting finding of this study is the correlation of disorganization with QOL, particularly regarding the aspect of “intrapsychic foundations”. This subscale identifies intrapsychic deficits that are seen as a core aspect of schizophrenia. The QLS intrapsychic foundations scale provides clinical judgment regarding intrapsychic elements in the dimensions of cognition, affectivity, and drive. A patient's sense of purpose, motivation, curiosity, empathy, ability to experience pleasure, and emotional interaction are assessed (Heinrichs et al., 1984). Intrapsychic foundations constitute the “starting blocks” from which the QLS dimensions measured by the other subscales are defined. Defects in these areas are reflected in impairments in the other three categories. For example, an alteration of empathy can cause problems in interpersonal relationships, and a deficit of drive can have consequences in finding and maintaining work. Each of the disorganization symptoms, comprising a variety of abnormalities in the organization of thought, speech, and attention, suggests a diminishment or absence of organization. There seems to be a loss of the ability to be directed toward or committed to a particular focal topic or goal. Such conditions are likely to impact patients' drives or motivations to initiate goal-directed activities that could yield pleasurable opportunities. Anhedonia and deficits in the dimensions of drive and motivation are supposed to underlie the inability to engage with other people in a manner that is mutually rewarding (Strauss, 2012), which lies at the core of the functional disability of people with schizophrenia and leads to various challenges, such as extreme social isolation. It should be reiterated that disorganization reflects a characteristic, underlying dimension close to the core of the disease.

The “instrumental role functioning” domain of the discrete QLS focuses on the role of a worker, student, or housekeeper/parent. Judgments are made about level of accomplishment, degree of underemployment given the person's talents and opportunities, and satisfaction derived from his/her role (Heinrichs et al., 1984). A large number of studies have identified a strong association between greater symptom severity and lower employment rates (McGurk et al., 2004, Bond and Drake, 2008 and Tsang et al., 2010). Patients in the present study had quite poor social and instrumental functioning, as evidenced by the low rate of employment (30%); disorganization may make occupational functioning much worse.

With regard to the second hypothesis, impaired verbal memory was related to a lower QOL. This finding is consistent with previous research and demonstrates a significant positive correlation between cognitive functioning and QOL. Studies have examined the role of cognitive variables in predicting social and community functioning, rehospitalization, vocational functioning, and QOL (Green et al., 2000). Verbal memory is among the strongest predictors of functional outcome and is associated with greater emotional discomfort, poorer QOL, worse clinical and community outcomes, improvement in work performance,

inefficient social problem solving, and worse performance of daily life skills (Toulopoulou and Murray, 2004).

Furthermore, we found a negative association between disorganization and verbal memory. Several cross-sectional studies have suggested that the performance on neurocognitive tests is correlated with major symptom factors, positive symptoms, negative symptoms, and disorganization (Addington and Addington, 1999, 2000; Brazo et al., 2002 and Brazo et al., 2005). Most of the previous studies found a stronger cross-sectional relationship with negative symptoms than with positive symptoms of the non-disorganizing type (Keefe et al., 2006a and Keefe et al., 2006b). A recent meta-analysis conducted by Ventura et al. (2010) demonstrated a moderate relationship between disorganization and neurocognition, while the relationship between neurocognition and reality distortion was relatively weak. In this study, the authors found evidence that disorganization was related to all of the examined domains of cognitive functioning. This finding suggested that disorganization represents a separate set of positive symptoms from those associated with reality distortion and has independent links to neurocognition.

Finally, when verbal memory was inserted into the model as a mediating variable of the relationship between disorganization and QOL, we found evidence that verbal memory was a partial mediator of this relationship. Starting from the results of our mediation analysis, we can suggest that disorganization affected QOL both directly and indirectly via verbal memory. Our work contributes to a broad literature base that highlights the strength and importance of the psychopathological and neurocognitive symptoms in influencing QLS. Velligan et al. (1997) reported a path model in which cognition predicted both the concurrent symptomatology and activities of daily living. Bowie et al. (2006), utilizing a composite scale for neurocognition, reported that neuropsychological performance predicted functional capacity, which predicted the three domains of real-world functioning. Furthermore, three recent studies assessed the magnitude of the associations of psychiatric symptoms and neurocognition with the QLS. In the study of Lipkovich et al. (2009), the processing speed demonstrated direct and indirect effects via negative symptoms on three domains of functioning measured by the QLS at baseline and following 24 weeks of antipsychotic treatment. In the study of Mohamed et al. (2008), social or occupational functioning was significantly and independently associated with measures of both neurocognition and symptoms. Perlick et al. (2008), using data from a large randomized Department of Veterans Affairs trial of antipsychotic medication for schizophrenia, suggested that symptoms and neurocognition both have independent associations with functioning; in fact, symptoms may be even more strongly associated with functioning than neurocognition. More recently, Pandina et al. (2013) demonstrated that improved cognition was significantly correlated with positive changes in clinical and functional status in subjects with schizophrenia or schizoaffective disorder. This may be linked to improvement in disorganized thoughts. In fact, in their study the neurocognitive composite score decreased by an estimated 0.81 unit when the PANSS disorganized thoughts factor score increased by 1 point.

A possible hypothesis to explain our finding is that verbal memory impairment and disorganization symptoms may be related to schizophrenia patients' deficits in cognitive control. Phillips and Silverstein (2003) have proposed that diverse cognitive dysfunctions may be related to dysfunctional coordination of the neural activity associated with contextually related stimuli, and that this underlies the phenomenological disorganization of mental processes in schizophrenia. Deficits in cognitive control could lead to the selection of inappropriate behavioral representations for ongoing actions in a manner that is likely to impact patients' social functioning (Chambon et al., 2008). Second, as suggested by Lysaker and Buck (2007), reduced memory functions could limit the acquisition of skills and the development of a rich

personal narrative. Such conditions could lead to a habitually avoidant style of coping and a negatively modified self-concept, with a number of important implications on social functions and QOL.

Our study has a number of limitations that should be highlighted. First, its cross-sectional nature did not allow us to clarify the direction of causality in the observed disorganization–cognitive function–QOL relationships. Second, to be eligible for this study, patients had to meet the criteria for psychiatric stability and were taking medications. Consequently, they were not representative of patients in acute phases of the disease or in other clinical settings. Finally, in the discussion of our findings, we need to consider the possible limitations of the instrument we chose to explore QOL. We decided to use the QLS because it is considered a gold standard research instrument for the assessment of QOL in severely ill schizophrenia patients when administered by trained clinical raters (Cramer et al., 2000). The QLS is a "disease-specific" instrument that provides an "external assessment" of the QOL based on the patients' self-reports and perspectives, as well as the clinician's professional judgment about the patient's functioning and life circumstances. However, two main limitations of the QLS should be considered. First, because the QLS was initially devised as a measure of schizophrenic deficit syndrome, it has been suggested that apathy and other negative symptoms have substantial theoretical overlaps with certain constructs evaluated by the QLS, especially within the IF subscale. Second, the possibility of measurement overlaps between QOL and disorganization should be considered. Clinical judgment is involved in both QLS and PANSS, and one must be cautious of circular interpretations. Disorganization was the strongest symptom predictor of QLS in the sample after backward selection, accounting for 30.3% of the variance in the total QLS score in our sample. Although this finding may be interpreted in terms of measurement redundancy, it has been suggested that there is little reason to use a QOL scale that fails to detect the impact of symptoms specific to schizophrenia (Awad et al., 1997). Moreover, QLS and PANSS ratings were not obtained by independent raters, and information given in one interview could affect the assessment of another interview. An alternative, or complementary, approach would be to assess functioning through patient self-reports of subjective QOL. Indeed, it was reported that, in patients with schizophrenia, the subjective rating of QOL may be valid and informative in assessing life satisfaction (Jung et al., 2010). Thus, future studies that further explore the issue of the determinants of subjective and objective QOL in schizophrenia patients are needed.

Despite these limitations, there are some strengths of this study that should be noted. First, we decided to focus on disorganization, which is considered an important feature of schizophrenia but has been widely neglected in studies of QOL. Second, our study was conducted in a stable, homogeneous community sample that was reflective of baseline levels of functioning and impairment. This point is particularly important due to the presence of systematic differences in how QOL interacts with psychiatric symptoms among mixed samples of inpatients and outpatients or early course and chronic patients. Ignoring these differences would obscure the results (Eack and Newhill, 2007). Finally, the type of analysis conducted allowed us to explore possible moderators of the effect of psychiatric symptoms on QOL.

Taken together, the results of our study suggest that disorganization and QOL are associated in a manner partially mediated by verbal memory. Current antipsychotics show a greater efficacy for treating delusions and hallucinations than conceptual disorganization or cognitive impairments. A variety of psychological and social interventions are needed to optimize recovery and should constitute an essential part of schizophrenia treatment (cognitive–behavioral therapy, social skills training, family psychoeducation, assertive community treatment, and supportive employment). We can conclude that greater attention must be given to the systematic investigation and treatment of these symptoms, as the QOL in stable schizophrenia may be improved by interventions targeting disorganization and verbal memory. Finally, we found a differential impact of disorganization on the dimensions of QOL, suggesting that, in schizophrenia,

the dimensions of different symptoms could be related to specific QOL domains. In the future, further investigations conducted on different samples of patients and with different experimental designs are needed to confirm this hypothesis.

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Contributors

MS, GR and PR designed the study and wrote the protocol. BC, FC, MG and CM carried out the patient clinical assessment and recruitment, data collection and analysis. CM and MS wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

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Table 1.

Demographic and clinical feature of the sample.

Demographic characteristics	
Sample (N)	276
Gender M/F	116/160
Age (years)	40 ± 10.8
Education (years)	12.12 ± 3.24
Psychiatric assessment	
Duration of illness (years)	14.2 ± 9.74
Paranoid subtype	158
Disorganized subtype	27
Undifferentiated subtype	57
Residual subtype	34
CGI-S	4.19 ± 1.13
PANSS	69.8 ± 23.7
QLS	65.1 ± 23.4
Neuropsychological assessment	
Stroop CW	20.34 ± 6.81
CVLT 1–5	39.19 ± 11.61
WCST cat	5.00 ± 1.69
TMT B–A	59.21 ± 21.9

Abbreviations: CGI-S = Clinical Global Impression-Severity Scale; PANSS = Positive and Negative Syndrome Scale; QLS = Quality of life Scale; Stroop CW = the number of colors named in the conflicting card at the Stroop Test; CVLT 1–5 = the total number of items correctly recalled over five learning trials at the California Verbal Learning Test; WCST cat = the number of achieved sorting categories at the Wisconsin Card Sorting Test; TMT B–A = the difference between TMT-B and TMT-A times at the Trail Making Test.

Table 2.
Univariate linear regression analyses among variables of interest (disorganization, neurocognition and QLS total score and single domains) and between these variables and potential confounders (age, education, positive symptoms, negative symptoms, excitement and emotional distress). Data were represented with standardized β.

IRNS (9)	QLS (8)	Emot distress	Excitement (6)	Disorganization(5)	Negative (4)	Positive (3)	Education (2)	Age (1)	
− 0.26***	− 0.21**	− 0.02	0.43	0.15*	0.09	0.10	–	–	1
− 0.01	0.15*	− 0.01	− 0.09	− 0.15*	0.08	− 0.09	–	–	2
− 0.36***	− 0.38***	0.48***	0.61***	0.61***	0.24***	–	− 0.09	0.10	3
− 0.54***	− 0.52***	0.28***	0.21***	0.63***	–	0.24***	0.08	0.09	4
− 0.49***	− 0.55***	0.47***	0.57***	–	0.63***	0.61***	− 0.15*	0.15*	5
− 0.25***	− 0.27***	0.47***	–	0.57***	0.21***	0.61***	− 0.09	0.04	6
− 0.30***	− 0.33***	–	0.47***	0.47***	0.28***	0.48***	− 0.01	− 0.02	7
–	–	− 0.33***	− 0.27***	− 0.55***	− 0.52***	− 0.38***	0.15*	− 0.21**	8
–	–	− 0.30***	− 0.25***	− 0.49***	− 0.54***	− 0.36***	− 0.01	− 0.26***	9
–	–	− 0.27***	− 0.22***	− 0.42***	− 0.31***	− 0.28***	0.05	− 0.05	10
–	–	− 0.25***	− 0.18**	− 0.44***	− 0.49***	− 0.25***	0.18**	− 0.15*	11
–	–	− 0.03	− 0.08	− 0.10	− 0.10	− 0.14*	0.07	0.03	12
0.29***	0.27***	− 0.19**	− 0.19**	− 0.42***	− 0.24***	− 0.27***	0.20**	− 0.37***	13
0.30***	0.37***	− 0.16*	− 0.17**	− 0.46***	− 0.28***	− 0.20**	0.22***	− 0.26***	14
0.03	0.10	− 0.06	− 0.07	− 0.19**	− 0.11	− 0.06	0.21***	− 0.06	15
− 0.25***	− 0.20**	0.18**	0.13*	0.20**	0.17**	0.2*	− 0.23***	0.06	16

	IRF (10)	IF (11)	COA (12)	Stroop CW (13)	CVLT 1–5 (14)	WCSTcat (15)	TMT b–a (16)
1	– 0.05	– 0.15*	0.03	– 0.37***	– 0.26***	– 0.06	0.06
2	0.05	0.18**	0.07	0.20**	0.22***	0.21***	– 0.23***
3	– 0.28***	– 0.25***	– 0.14*	– 0.27***	– 0.20**	– 0.06	0.2*
4	– 0.31***	– 0.49***	– 0.10	– 0.24***	– 0.28***	– 0.11	0.17**
5	– 0.42***	– 0.44***	– 0.10	– 0.42***	– 0.46***	– 0.19**	0.20**
6	– 0.22***	– 0.18**	– 0.08	– 0.19**	– 0.17**	– 0.07	0.13*
7	– 0.27***	– 0.25***	– 0.03	– 0.19**	– 0.16*	– 0.06	0.18**
8	–	–	–	0.27***	0.37***	0.10	– 0.20**
9	–	–	–	0.29***	0.30***	0.03	– 0.25***
10	–	–	–	0.25***	0.27***	0.03	– 0.12*
11	–	–	–	0.18**	0.33***	0.12*	– 0.13*
12	–	–	–	0.02	– 0.02	0.07	– 0.00
13	0.25***	0.18**	0.02	–	–	–	–
14	0.27***	0.33***	– 0.02	–	–	–	–
15	0.03	0.12*	0.07	–	–	–	–
16	– 0.12*	– 0.13*	– 0.00	–	–	–	–

Abbreviations: Positive = positive symptoms; Negative = negative symptoms; Emot distress = emotional distress; QLS = Quality of life Scale; IRSN = interpersonal relations and social network; IRF = instrumental role functioning; IF = intrapsychic foundations; COA = common objects and activities; Stroop CW = the number of colors named in the conflicting card at the Stroop Test; CVLT 1–5 = the total number of items correctly recalled over five learning trials at the California Verbal Learning Test; WCST cat = the number of achieved sorting categories at the Wisconsin Card Sorting Test; TMT B–A = the difference between TMT-B and TMT-A times at the Trail Making Test.

* = $p < 0.05$.
** = $p < 0.01$.
*** = $p < 0.001$.

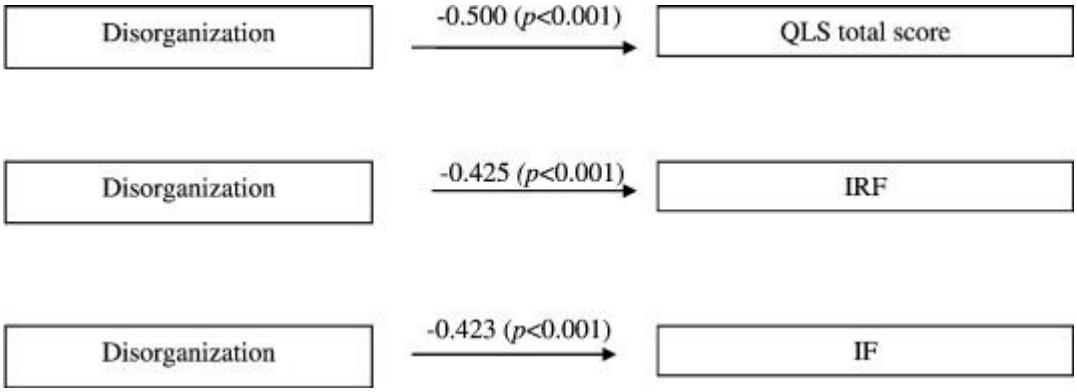

Fig. 1. Mediational analyses (first step).
The figure shows the effect of disorganization on QOL total score, IF and IRF.

Abbreviations: QLS = Quality of life Scale; IRF = instrumental role functioning; IF = intrapsychic foundations. Paths were represented with standardized Beta.
Note: age, education, clinical (positive, negative, excitement, emotional distress) and cognitive variables have been partialed out with multiple regression.

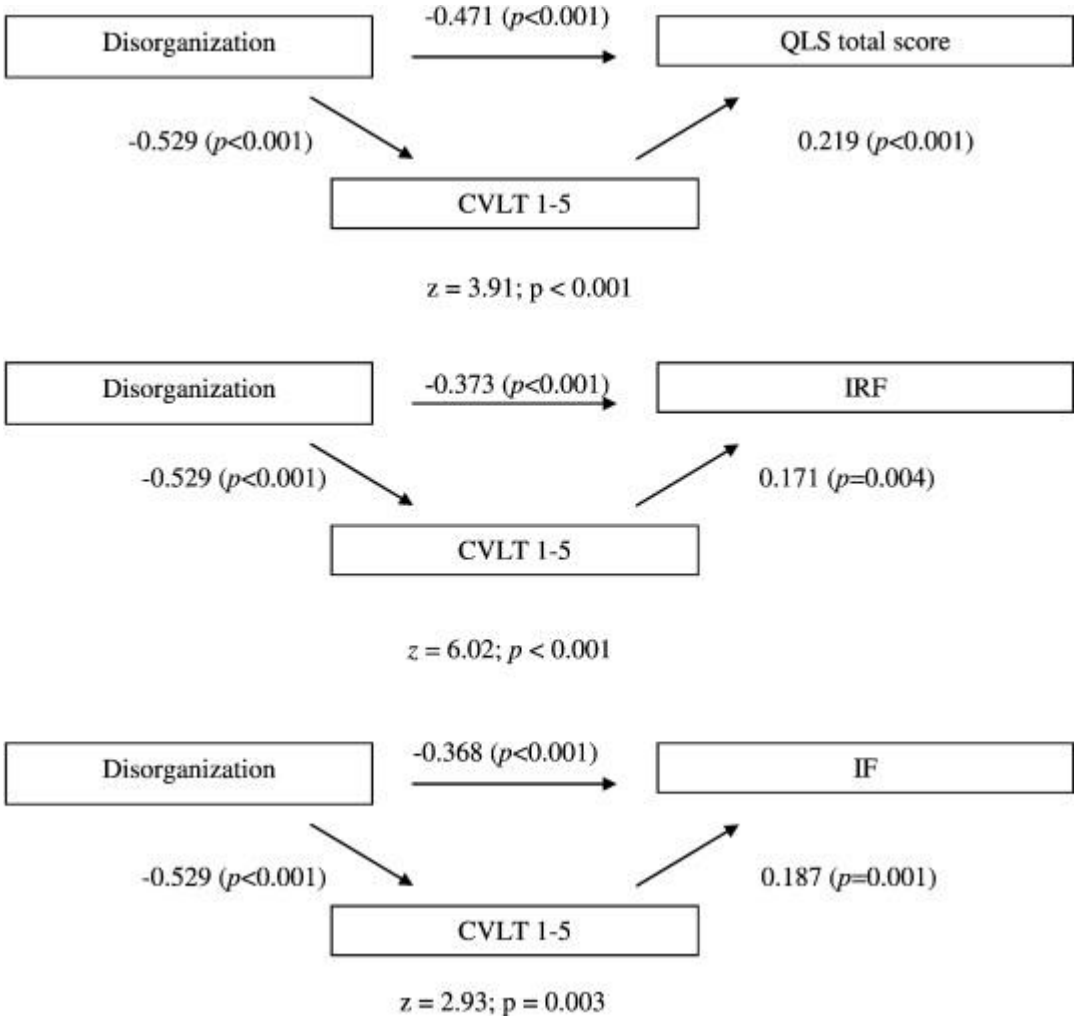

Fig. 2. Mediational analyses (second step).

The figure shows the indirect effects of disorganization on QLS total score, IRF and IF. Paths were represented with standardized Beta.

Abbreviations: QLS = Quality of life Scale; IRF = instrumental role functioning; IF = intrapsychic foundations; CVLT 1–5 = the total number of items correctly recalled over five learning trials at the California Verbal Learning Test.

Note: age, education, clinical (positive, negative, excitement, emotional distress) and cognitive variables have been partialed out with multiple regression.

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