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Relative contributions of negative symptoms, insight, and coping strategies to quality of life in stable schizophrenia

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Abstract

The purpose of this cross-sectional study was to examine the relative contributions of negative symptomatology, insight, and coping to quality of life (QOL) in a sample of 92 consecutive outpatients with stable schizophrenia referring to the Department of Neuroscience, Psychiatric Section, University of Turin, Struttura Semplice di Coordinamento a Valenza Dipartimentale (SSCVD), Department of Mental Health ASL TO1, Molinette, Italy, in the period between July 2009 and July 2011. In order to assess the specific effect of negative symptoms on QOL and the possible mediating role of insight and coping, two mediation hypotheses were tested, using multiple regression analyses specified by Baron and Kenny (1986). Our findings suggest that (a) higher negative symptoms predict a worse Quality of Life Scale (QLS) intrapsychic foundations (IF) subscale score; (b) attribution of symptoms and coping-social diversion have a direct and positive association with QLS-IF; (c) patients high in negative symptoms are less likely to use attribution of symptoms and coping-social diversion; and (d) attribution of symptoms and coping-social diversion act as partial mediators in the negative symptoms-QOL relationship. The prediction model accounts for 45.3% of the variance of the QLS-IF subscale score in our sample. In conclusion, our results suggest that insight and coping-social diversion substantially contribute to QOL in patients with higher negative symptoms. These factors are potentially modifiable from specific therapeutic interventions, which can produce considerable improvements in the QOL of this population.

Keywords: Attribution of symptoms; Coping social diversion; Negative symptoms; Quality of life; Schizophrenia.

1. Introduction

Despite the general agreement that schizophrenia patients have impaired quality of life (QOL) compared with members of the general population (Lehman, 1988, Sullivan et al., 1991, Ritsner et al., 2000, Saleem et al., 2002 and Alptekin et al., 2005), the determinants of QOL are poorly understood in this population (Tolman and Kurtz, 2012).

Moreover, even if some authors have shown that there are a few significant correlations between subjective and observer-rated QOL (Dickerson et al., 1998; Heider et al., 2007), also in first-time-admission schizophrenic patients (Górna et al., 2008), other ones have found that they are not closely related, and concluded that subjective and observer-rated QOL have different determinants in patients with schizophrenia (Fitzgerald et al., 2001). A recent review (Tomotake, 2011) highlighted that depressive symptoms are most related to subjective QOL, whereas negative symptoms are most associated with the observer-rated one, and basic life skills are related to both. Cognitive dysfunctions in some neurocognitive domains such as verbal memory, vocabulary, fluency performance, attention, social knowledge, and executive function are associated with lower observer-rated QOL, but the effects of them are much smaller than negative and depressive symptoms. Nonetheless, it was suggested that the magnitude of the relationship between clinical symptoms and QOL is not large and it is influenced by several factors, such as patient characteristics, stage of illness (acute versus chronic samples), and treatment setting (community versus inpatients units) (Eack and Newhill, 2007).

Lastly, since QOL in schizophrenia appears to be a complex outcome encompassing several major dimensions (including psychological status, functional abilities, subjective wellbeing, social interactions, economic status, vocational status, and physical status) and multiply determined with no single predictor variable explaining a sufficient amount of variance, recent research has focused on the identification of mediators or moderators between clinical variables and QOL.

Among them, insight into illness could be particularly relevant because preserved insight had been suggested to be a predictive value for the treatment outcome in schizophrenia, especially when improving adherence to treatment and reducing the risk of relapse and re-hospitalization (Amador et al., 1994 and Quee et al., 2011). Contradictory findings have been reported concerning the relationship between insight and QOL in patients with schizophrenia (Karow et al., 2007). Whereas previous studies have shown an association of increased insight with better expert-rated QOL (Dickerson et al., 1997, Schwartz, 1998, Hasson-Ohayon et al., 2006, Aghababian et al., 2011 and Kurtz and Tolman, 2011), other studies have demonstrated an inverse relationship between insight and subjective QOL (Ritsner, 2003, Sim et al., 2004, Hasson-Ohayon et al., 2006 and Boyer et al., 2012) and other ones have failed to find an association (Browne et al., 1998, Williams and Collins, 2002 and Hofer et al., 2006). The direction of the relationship between insight and QOL, which can appear paradoxical, should be explored by taking into account the multidimensional aspect of insight and potential confounding factors.

As for the relationship between negative symptoms and insight, studies included in the review of Mañkinen et al. (2008) reported that overall, patients with negative symptoms may have poor awareness of the adverse effects of their symptoms. A meta-analysis of 40 published English-language studies (Mintz et al., 2003) indicates that there is a small negative relationship between both positive and negative symptom severity and insight, with age of onset and acute versus chronic disease status serving as moderating variables, and that 3–7% of the variance in insight is explained by severity of symptomatology in schizophrenia patients.

Coping resources are considered a crucial factor potentially mediating the effects of stressors on QOL outcomes. Researchers have frequently classified coping strategies into three categories: problem focused (i.e. strategies to actively solve an underlying problem, cognitively reconceptualize it and potentially minimize its adverse effects), emotion-focused (i.e. strategies to restructure cognitions to modify the emotional response), and avoidance-focused (avoidant-distracted coping, i.e. strategies to avoid a stressful situation via self-distraction from stressful situation, e.g. “giving up” denial, or engaging in a substitute task; avoidant-social coping, i.e. strategies to avoid a stressful situation by using social diversion, i.e. choosing to be with other people and seeking emotional support) (Folkman and Lazarus, 1980). Although there is no consensus regarding which coping strategies are more or less adaptive and most effective in reducing psychopathological and distress symptoms (Aldwin and Revenson, 1987, Carr, 1988, Thoits, 1995, Lazarus, 2000 and Austenfeld and Stanton, 2004), schizophrenia patients have been found to use less effective coping strategies to deal with stress than non psychiatric controls (Wield et al., 1990, Van Den Bosch et al., 1992 and Horan et al., 2005). They generally use more passive emotion-focused coping strategies, such as avoiding, ignoring, and not thinking about the problem (Mueser et al., 1997, Jansen et al., 2000, Wilder-Willis et al., 2002, Aghevli et al., 2003 and Phillips et al., 2009). The use of such coping strategies can explain why schizophrenia patients report greater dissatisfaction with all aspects of their lives (i.e. lower QOL) (Rudnick and Kravetz, 2001 and Ritsner et al., 2003), but more research is required to elucidate this relationship.

Moreover, according to the integrated model of the determinants of functioning and well-being in schizophrenia (Yanos and Moos, 2007) psychiatric factors are hypothesized to exert a moderate influence on coping responses. Patients' symptom severities were related to maladaptive coping patterns (Wiedl, 1992, Lee et al., 1993, Strous et al., 2005, Lysaker et al., 2006 and Lee et al., 2011). The relationship between a higher level of negative symptoms and the more reliance on emotion-focused coping was repeatedly reported in studies of schizophrenia patients (Wiedl, 1992, Hultman et al., 1997, Wilder-Willis et al., 2002, Lysaker et al., 2006, Martins and Rudnick, 2007 and Rudnick and Martins, 2009). Subjects with severe negative symptoms might have difficulties in using a problem-focused coping because it demands volition, attention, and more cognitive functions (Wilder-Willis et al., 2002 and Lysaker et al., 2004). Tsai et al. (2010) have found that clients with particularly high negative symptoms are more isolated, and engage in more maladaptive coping than others. Meanwhile, subjects who relied on maladaptive coping strategies would not be tolerable to various stressful circumstances, and as a consequence, they could be more depressed, anxious, and symptomatic (e.g. avoid social interactions). However, evidence is mixed.

Previous research has linked negative symptoms to coping strategies and insight, and coping strategies and insight to QOL, but in separate studies.

1.1. The current study

The present study was conducted to determine whether the relationship between negative symptoms and QOL might be mediated by the extent of insight and coping strategies in patients with stable schizophrenia. To the best of our knowledge, we are the first to report on this issue in a sample of outpatients with stable schizophrenia. Indeed, although the relation between some of the disease variables and QOL has been described in the literature, the pattern of interaction between the different factors and the specific contribution of each alteration to QOL remains to be clarified.

Despite the field of QOL in schizophrenia has witnessed significant growth in the number of publications over the past two decades, a recent review by Awad and Voruganti (2012) has concluded that a uniform definition may not be possible, and instead, it may be preferable to have several

definitions, which may enrich the concept and broaden its usefulness. The absence of agreement on QOL has led to the proposal of often unclear and overlapping definitions, with corollaries to a multitude of QOL instruments (Boyer et al., 2013). Despite several reviews of literature on QOL instruments (Simeoni et al., 2000, Bobes et al., 2005 and Awad and Voruganti, 2012), the authors generally consider that there is little guidance to choose the most appropriate questionnaires. A ‘best scale’ for the measurement of QOL does not exist (Awad and Voruganti, 2012). There are, however, instruments that are best suited to a particular purpose (Hyland, 2002). The Heinrichs–Carpenter QLS is considered one of the most frequently used observer-rated QOL measures, specifically constructed to measure QOL of community dwelling outpatients with schizophrenia. The QLS combines the subjective patient report and objective data via assessment of the patients’ internal state and the clinician’s professional judgment about the patient’s functioning and life circumstances. It could be considered a gold standard research instrument for assessment of QOL in severely ill schizophrenia patients when administered by trained clinical raters (Cramer et al., 2000). This QLS has been reported to be acceptable in terms of these measures of validity (Lehman et al., 1993 and Lehman, 1996) and to show substantial sensitivity to subtle change and treatment effects (Rosenheck et al., 1998 and Mohamed et al., 2008). For the purposes of the present study, we were interested in one of the four subscales of the QLS, intrapsychic foundations (IF). The IF subscale is the key domain of QLS, which is based entirely on the schizophrenia patient’s intrapsychic subjective elements that are seen as a core aspect of schizophrenia. The IF subscale gives a clinical judgment regarding intrapsychic elements in the dimensions of cognition, affectivity, drive. Patient’s sense of purpose, motivation, curiosity, empathy, ability to experience pleasure, and emotional interaction are assessed (Heinrichs et al., 1984). They reflect the propensity of subjects to formulate their goals, future plans and drive to achieve them. These items may be most relevant to the richness and fullness of the inner life and expressiveness of the patient, with no clear relationship to measures of external functioning. Moreover, the IF subscale constitutes the “starting blocks” from which QLS dimensions measured by the other subscales are defined. Defects in these areas reflect impairments in the other three QLS subscales, for example, alteration of empathy can cause problems in interpersonal relationships; deficit of drive can have consequences in finding and maintaining a work; and so on. Such conditions are likely to impact on patients’ drive or motivation to initiate goal-directed activities that can 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, leading to various difficulties, such as extreme social isolation. Lastly, as reported in other studies (Mohamed et al., 2008, Perlick et al., 2008 and Song et al., 2011), we used a newly constructed modification of the PANSS negative syndrome scale that eliminated three items (including emotional withdrawal, passive/apathetic withdrawal, and difficulty in abstract thinking) most directly overlapping with measures of community functioning, which was suggested strategy to avoid the redundancy of common variance between the negative symptoms and QLS scores. Thus, the objectives and hypotheses of the current study were threefold.

First, we investigated the ability of negative symptoms alone to predict QOL. Given the results of previous studies, we expected that their severity would significantly predict a worse QOL. Second, we studied the ability of the two dimensions of insight and coping strategies to predict QOL. Given the previous studies, we expected a role for both of them.

Third, we investigated whether negative symptoms continued to predict QOL when both insight and coping strategies were also considered. It was expected that negative symptoms, insight and coping strategies interact in influencing QOL, insight and coping strategies being partial mediators of the relationship between negative symptoms and QOL.

2. Materials and methods

2.1. Participants

The study has been conducted at the Department of Neuroscience, Psychiatric Section, University of Turin, Struttura Semplice di Coordinamento a Valenza Dipartimentale (SSCVD), Department of Mental Health ASL TO1, Molinette, Italy, in the period between July 2009 and July 2011.

Patients were initially evaluated by a clinician-psychiatrist, and if they met Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) (APA, 2000) criteria for schizophrenia, they were seen subsequently by our research team (C.M. and T.F.). Of these, a sample of consecutive subjects routinely treated in a community setting and fulfilling the following criteria was included in the study:

1. men and women in the 18–65 years age group;
2. diagnosis of schizophrenia according to the DSM-IV-TR, confirmed by two expert clinicians (C.M. and T.F.) using the Structured Clinical Interview for DSM-IV disorders (SCID) (First et al., 1997). The two psychiatrists were aware of previous diagnosis and they could also review the previous clinical charts, available for all the patients. Subjects were excluded if they had a current disorder other than schizophrenia on Axis I of the DSM-IV-TR, a current or past codiagnosis of autistic disorder or another pervasive developmental disorder, a history of severe head injury (coma $48 \geq$ hours), and a diagnosis of organic disorder (especially neurological);
3. patients with stable schizophrenia, i.e. patients had been clinically stable for at least 6 months as judged by treating psychiatrist (during this period all patients had to be treated as outpatients, treatment regimen had not been modified, and there was no essential change in psychopathology). The choice of antipsychotic drug prescribed and dosage was left to the discretion of the treating physicians, which happened well before the initiation of the study.

Patients were evaluated using a semistructured interview to assess demographic features. Data were collected to determine age, gender, education, age at onset of schizophrenia (report of first contact with a psychiatric service), length of illness, and antipsychotic treatment. All patients were submitted to standard care provided in community mental health centers in Italy (pharmacological treatment, clinical monitoring at least on a monthly basis, home care when required, and psychosocial and rehabilitation interventions tailored to patient's needs).

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

2.2. Psychiatric assessment

2.2.1. Study design and assessment instruments

Overall severity of illness was rated using the Clinical Global Impression-Severity scale, CGI-S (Guy, 1976). Current levels of psychopathological symptoms were assessed using the Positive and Negative Syndrome Scale (PANSS), which includes Positive Symptoms (PANSS-P), Negative Symptoms (PANSS-N), and General Psychopathology (PANSS-G) subscales (Kay et al., 1987). For the specific purpose of our study we used a newly constructed modification of the PANSS negative syndrome scale.

Depressive symptoms were evaluated using the Calgary Depression Scale for Schizophrenia (CDSS) (Addington et al., 1990), specifically developed to distinguish depressive symptoms in schizophrenia rather than positive or negative symptoms or antipsychotic-induced side effects.

To quantify the global functioning of patients, we used the Global Assessment of Functioning scale (GAF) (Jones et al., 1995). The GAF evaluates functioning across three domains (psychological, social functioning and occupational/educational functioning) on a hypothetical continuum of mental health-illness. For the purpose of our study, raters were instructed to use the GAF to measure only psychosocial functioning in the month before rating, as reported in other studies (Altshuler et al., 2002, Martinez-Aran et al., 2004 and Martinez-Aran et al., 2007).

Insight was measured with the Scale to assess the Unawareness of Mental Disorder (SUMD) (Amador and Strauss, 1990). For the purpose of our study, we chose to use the sum of the measures of awareness of current symptomatology and attribution of symptoms as these dimensions are thought to be distinct and to provide the broadest assessment of insight of illness (Larøi et al., 2000). Awareness and attribution are evaluated in each one of 17 items aimed at specific symptoms. Thus, two subscales are made up: that of awareness of the symptoms which is the mean of the sums of the scores according to the number of items scored and that of attribution of the symptoms which is the mean of the scores of the symptoms that can be assessed because the patient is aware of them. For the purpose of the present research, data analysis was primarily focused on current awareness and attribution of symptoms at the time of testing.

Self-esteem was measured using the Rosenberg Self-Esteem Scale (RSES) (Rosenberg, 1965). This is a 10 item self-administered questionnaire with items answered on a four-point scale from strongly agree (rated 3) to strongly disagree (rated 0). The scores range from 0 to 30. Scores between 15 and 25 are within normal range; scores below 15 suggest low self-esteem.

Coping was measured using the Coping Inventory for Stressful situations (CISS) (Endler and Parker, 1990), an easily, valid and reliable administered scale for measuring multidimensional coping. The CISS is a 48-item questionnaire assessing three coping dimensions: Task-Oriented coping, Emotion-Oriented coping, and Avoidance, which is constituted by two subscales, Social Diversion and Distraction. Subjects rate 48 items on a five-point-Likert scale from not at all to very much indicating how much they engage in each kind of activity when they encounter a difficult, upsetting, and stressful situation. Both Italian validations of the CISS (Pedrabissi and Santinello, 1994 and Sirigatti et al., 1996) confirmed the original factorial structure.

To assess QOL, we used Heinrich's Quality of life Scale (QLS) (Heinrichs et al., 1984), which is a 21-item semi-structured interview used by trained raters to assess functioning based on the patient's self-report and the rater's judgement. Each item is rated by a six-point Likert scale on which higher scores indicate a higher level of functioning. For the specific purpose of the study we chose to focus on the IF subscale.

In order to index executive functions, we used the number of perseverative errors and the number of completed categories on the Wisconsin Card Sorting Test (WCST) (Heaton et al., 1993). The WCST requires the subject to match a stimulus card with one out of four key cards according to certain matching principles (shape, color, and number of object). The subject should switch from a previous correct category upon receiving negative feedback to look for a new rule after 10 correct responses. To understand the cognitive processing during the WCST, one needs to discriminate when the subject is correctly sorting cards and when the subject is incorrectly and perseveratively sorting cards. For the purpose of our analysis we chose to use the number of achieved sorting categories, which is usually regarded as the main benchmark for the evaluation of WCST (Kawai et al., 2006).

Clinical assessment was carried out in two sessions, the first for the administration of SCID and the second for the administration and scoring of other clinical scales. All assessments (SCID and psychopathological rating scales) were performed by experienced psychiatrists (C.M. and T.F.). Prior to this study, interviewers received training sessions for SCID. In an attempt to reduce inter-rater variability, all raters were trained to administer the psychometric tools according to common standards. Also prior to the commencement of the present study, they participated in a pilot study in order to reach a consensus on 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 in order to reach consensus ratings. In this study, the agreement-within one point-between the raters varied from 79% to 91% of the time for all items on PANSS; 93% of the time for SUMD total score; and 91% of the time for QLS total score. Efforts were made to maintain inter-rater reliability across the entire study period, including careful calibration and standardization procedures and regular, in-depth review of a sample of interviews with the lead author.

WCST was administered by a trained clinical psychologists (F.C.) who was unaware of clinical characteristics and results of psychiatric rating scales.

2.3. Data analysis

Analyses were planned in the following three stages:

In stage 1, univariate linear regressions were calculated to examine the relationship among QLS-IF and demographic, clinical and neuropsychological data.

In stage 2, all clinical variables that were significantly associated with QLS-IF in the univariate analyses at $p < 0.05$ level were subsequently analyzed using a stepwise multiple regression with a backward procedure to test their contribution to QLS-IF. 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, two mediation hypotheses were tested, using multiple regression analyses 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 errors (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: (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 negative symptoms on the QLS-IF score (i.e. the product of the

total negative symptoms→M and M→QLS-IF score pathways) and a test of a decrease in the total effect of negative symptoms on the QLS-IF score 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

Ninety-two consecutive outpatients who met the inclusion criteria were enrolled in the study; 50 (54.%) were males and 42 (46%) were females. They had a DSM IV-TR diagnosis of schizophrenia paranoid subtype (53, 57%), disorganized subtype (22, 24%), undifferentiated subtype (9, 10%), and residual subtype (8, 9%). The mean age (\pm S.D.) was 42.9 (\pm 11.4) years, mean education (\pm S.D.) was of 11.0 (\pm 3.24) years. The mean average duration of illness (\pm S.D.) was 16.8 (\pm 11.1) years. The average number of previous hospitalizations in our sample was 4.28 (3.89). Seventy-three (79%) patients were treated with SGAs, 19 (21%) were under neuroleptics.

Socio-demographic and clinical characteristics of patients' population are shown in Table 1. We performed linear regressions for QLS-IF scores with any clinical variable assessed. These analyses were performed to provide a preliminary screening of appropriate candidate variables for entry into a subsequent regression model, as described below. Based on those preliminary univariate associations, $p < 0.05$ was adopted for inclusion in the regression model. The following variables were selected for QLS-IF model, including duration of illness, PANSS-N, PANSS-G, CGI, SUMD-attribution, SUMD-awareness, GAF, Coping-task oriented, Coping-emotion oriented, Coping-social diversion, and Coping-distraction (Table 2).

Table 1. Sociodemographic and clinical characteristics of the sample.

Age. years. mean (\pmS.D.)	42.9 (\pm 11.4)
Education. years. mean (\pmS.D.)	11.0 (\pm 3.24)
Duration of illness. years. mean (\pmS.D.)	16.8 (\pm 11.1)
PANSS-P. mean (\pmS.D.)	13.7 (\pm 5.89)
PANSS-N. mean (\pmS.D.)	19.7 (\pm 7.77)
PANSS-G. mean (\pmS.D.)	33.6 (\pm 8.66)
CGI. mean (\pmS.D.)	4.52 (\pm 0.95)
CDSS. mean (\pmS.D.)	4.53 (\pm 4.81)
SUMD-attribution. mean (\pmS.D.)	3.36 (\pm 1.14)
SUMD-awareness. mean (\pmS.D.)	3.12 (\pm 1.01)
GAF. mean (\pmS.D.)	55.9 (\pm 13.6)
OLS-IF. mean (\pmS.D.)	21.3 (\pm 7.76)
Rosenberg self-esteem. mean (\pmS.D.)	27.6 (\pm 5.74)
CISS. task oriented. mean (\pmS.D.)	50.5 (\pm 12.3)
CISS. emotion oriented. mean (\pmS.D.)	43.8 (\pm 13.3)
CISS. social diversion. mean (\pmS.D.)	14.1 (\pm 5.02)
CISS. distraction. mean (\pmS.D.)	18.2 (\pm 6.83)
WCST. number of preservative errors. mean (\pmS.D.)	15.3 (\pm 14.4)
WCST, number of completed categories, mean (\pmS.D.)	4.93 (\pm 1.76)

PANSS-P: Positive and Negative Syndrome Scale, Positive Symptoms; PANSS-N: Positive and Negative Syndrome Scale, Negative Symptoms; PANSS-G: Positive and Negative Syndrome Scale, General Psychopathology; CGI: Clinical Global Impression Scale; CDSS: Calgary Depression Scale for Schizophrenia; SUMD: Scale to assess the Unawareness of Mental Disorder Scale; GAF: Global Assessment of Functioning; QLS-IF: Quality of Life Scale, Intrapsychic foundations; CISS: Coping Inventory for Stressful Situations; and WCST: Wisconsin Card Sorting Test.

Table 2. Exploratory univariate linear regressions between QLS-IF and socio-demographic and clinical variables.

	β^*	p
Age	-0.209	0.045
Education	0.233	0.027
Duration of illness	-0.298	0.004
PANNS-P	-0.001	0.990
PANNS-N	-0.595	0.000
PANNS-G	-0.341	0.001
CGI	-0.353	0.001
CDSS	-0.031	0.771
SUMD-attribution	-0.518	0.000
SUMD-awareness	-0.445	0.000
GAF	0.491	0.000
Rosenberg self-esteem	0.045	0.669
CISS, task oriented	0.311	0.004
CISS, emotion oriented	0.298	0.005
CISS, social diversion	0.476	0.000
CISS, distraction	0.038	0.000
WCST, number of preservative errors	-0.256	0.027
WCST, number of completed categories	0.277	0.017

PANSS-P: Positive and Negative Syndrome Scale, Positive Symptoms; PANSS-N: Positive and Negative Syndrome Scale, Negative Symptoms; PANSS-G: Positive and Negative Syndrome Scale, General Psychopathology; CGI: Clinical Global Impression Scale; CDSS: Calgary Depression Scale for Schizophrenia; SUMD: Scale to assess the Unawareness of Mental Disorder Scale; GAF: Global Assessment of Functioning; QLS-IF: Quality of Life Scale, Intrapsychic foundations; CISS: Coping Inventory for Stressful Situations; and WCST: Wisconsin Card Sorting Test.

After backward selection of variables, the combination of three predictor variables (i.e. PANSS-N, Coping social diversion, and SUMD-attribution) provided the best-fit QLS-IF model for the data. The sample adjusted R² for the model was 0.453, indicating that approximately 45.3% of the variance of the QLS-IF score in the sample could be accounted for by the combination of these three predictors (Table 3).

Table 3. Multiple regression with a backward stepwise procedure: contributors to QLS-IF.

Variable	β^*	t	p	adjustedR²**
PANSS-N	-0.358	-3.613	0.001	0.453
Coping-social diversion	0.348	4.147	0.000	
SUMD-attribution	-0.218	-2.229	0.029	

PANSS-N: Positive and Negative Syndrome Scale, Negative Symptoms; QLS-IF: Quality of Life Scale, Intrapsychic foundations.

*Standardized β .

**Adjusted R² for the entire model.

To better understand the pattern of correlations among negative symptoms, Coping social diversion, and SUMD-attribution, two mediational hypotheses were tested. Both mediational models, with standardized β s, are presented in Table 4 and Fig. 1.

Table 4. Regression models testing the mediation chains.

	β	SE	p	Adjusted R^2
Model 1				
PANSS-N→QLS-IF	-0.595	0.085	0.000	0.347
PANSS-N→Coping social diversion	-0.240	0.074	0.028	
Coping social diversion→QLS-IF	0.476	0.148	0.000	0.217
PANSS-N→QLS-IF excluding Coping social diversion	-0.476	0.090	0.000	0.426
Sobel test $z=-2.0289$, $p=0.0212$				
Model 2				
PANSS-N→QLS-IF	-0.595	0.085	0.000	0.347
PANSS-N →SUMD-attribution	0.084	0.013	0.000	
SUMD-attribution→QLS-IF	-0.518	0.611	0.000	0.261
PANSS-N→QLS-IF excluding SUMD-attribution	-0.444	0.100	0.000	0.388
Sobel test $z=-4.2946$, $p=0.00001750$				

PANSS-N: Positive and Negative Syndrome Scale. Negative Symptoms; QLS-IF: Quality of Life Scale. Intrapsychic foundations.

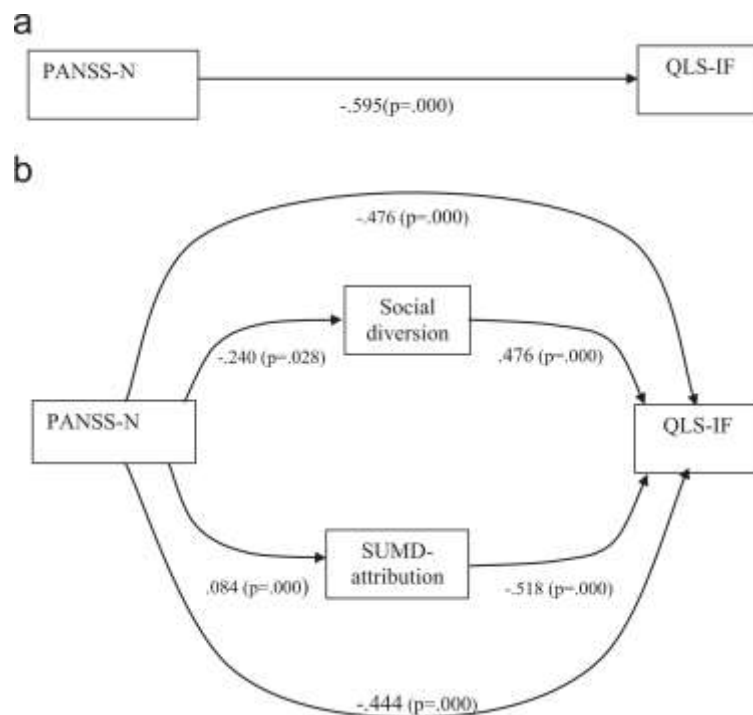


Fig. 1. Two mediational hypotheses. Standardized coefficients are shown for each path (with p in parentheses). PANSS-N: Positive and Negative Syndrome Scale, Negative Symptoms; QLS-IF: Quality of Life Scale, Intrapsychic foundations; SUMD: Scale to assess the Unawareness of Mental Disorder Scale.

In our case each step the IV was PANSS-N, the hypothetical Ms were Coping social diversion and SUMD-attribution, and the outcome variable, the DV, was QLS-IF.

In the first analysis, we tested the effect of negative symptomatology on QLS-IF (Fig. 1a). The effect of negative symptomatology was significant ($\beta=-0.595$, $SE=0.085$, $p=0.000$). In the second analysis, we inserted in the model Coping social diversion and SUMD-attribution as potential Ms of the effects of negative symptomatology (Fig. 1b). As can be seen in Fig. 1b and Table 3, negative symptomatology significantly predicts both Coping social diversion ($\beta=-0.240$, $SE=0.074$, $p=0.028$) and SUMD-attribution ($\beta=0.084$, $SE=0.013$, $p=0.000$). On the right side of the figure, it can be seen that both Coping social diversion ($\beta=0.476$, $SE=0.148$, $p=0.000$) and SUMD-attribution ($\beta=-0.518$, $SE=0.611$, $p=0.000$) significantly predict QLS-IF. The direct coefficient of negative symptomatology remained significant after inclusion of Coping social diversion and SUMD-attribution as mediating variables, while it changes somewhat in magnitude (β from -0.595 to -0.476 for Coping social diversion as potential M; and β from -0.595 to -0.444 for SUMD-attribution as potential M). Thus, part of the overall effect of negative symptomatology on QLS-IF appeared to be mediated both by Coping social diversion and SUMD-attribution (via indirect path mediated by Coping social diversion and SUMD-attribution). Sobel tests for mediation demonstrated that both Coping social diversion ($z=-2.0289$, $p=0.021$) and SUMD-attribution ($z=-4.2946$, $p=0.000$) significantly mediated the relation between negative symptomatology and QLS-IF.

4. Discussion

This study used a cross-sectional design and regression analyses to explore the complex relationships between negative symptoms, insight, and coping strategies in predicting QOL within a demographically representative sample of outpatients with stable schizophrenia, characterized by a reasonably chronic course, a high level of disability, and moderately severe positive and negative symptoms.

For the purpose of our analysis, we aimed to test three hypotheses. First, as hypothesized, the severity of negative symptoms was associated with a worse QOL score. A possible explanation of it can be that negative symptoms include a persistent reduction in the ability to express emotion, experience pleasure, initiate activities, and follow through with a course of action (Earnst and Kring, 1997, Möller, 2007 and Salvatore et al., 2007).

Such findings are consistent with past research using this scale showing a clear association between negative symptoms and QLS scores in cross-sectional analyses (Meltzer et al., 1990, Galletly et al., 1997, Milev et al., 2005, McGurk et al., 2000, Norman et al., 2000, Fitzgerald et al., 2001, Herbener and Harrow, 2004, de Souza and Coutinho, 2006, Tomotake et al., 2006, Kusel et al., 2007, Aki et al., 2008 and Narvaez et al., 2008; Rocca et al., 2009b; Fujimaki et al., 2012 and Lin et al., 2013) and in a set of longitudinal ones (Mohamed et al., 2008 and Rabinowitz et al., 2012). Considering that QLS was originally designed to assess deficit symptoms and dysfunctions related to these symptoms, a concept which is 'overlapping', although 'not co-extensive' with negative symptoms (Heinrichs et al., 1984 and Carpenter et al., 1988), the correlation between the severity of disabling negative symptoms and QLS scores seems reasonable. Moreover, it has been suggested that there is little point in using a QOL scale which fails to detect the impact of symptoms specific to schizophrenia (Awad et al., 1997).

In previous studies, this association was argued to partly reflect some redundancy of common variance between negative symptoms and QOL for individuals with schizophrenia. In contrast, our study found an association in spite of recalculation of negative symptoms according to the strategy suggested in previous studies to avoid redundancy. Indeed, to control for this overlap and to avoid collinearity and over-inflation of observed effects, some studies omitted portions of the QLS

(Rabinowitz et al., 2012), while others did not include negative symptoms (Swartz et al., 2003), or excluded some key negative factor symptoms (Mohamed et al., 2008, Perlick et al., 2008 and Song et al., 2011). There is some consistency between our findings and those of the abovementioned studies. Indeed, Rabinowitz et al. (2012), in a study using data from the National Institute of Mental Health CATIE trial of chronic schizophrenia, suggested that improvement in negative symptom factor might have distinctive and independent effects on functional outcome as assessed with selected items from the Heinrich's and Lehman's Quality of Life Scales measuring aspects of functioning that did not overlap with negative symptoms. Mohamed et al. (2008), in a previous CATIE publication, reported that negative symptoms are more highly correlated to functioning at the bivariate and multivariate levels than positive symptoms, being independently significant correlates and predictors of functioning. The authors excluded, as we did, key negative factor symptoms: "difficulty in abstracting," "emotional withdrawal," and "passive/apathetic social withdrawal," and examined PANSS subscales and not factors.

Moreover, the relative contribution of negative symptoms on QOL may depend on the sample that is being studied, i.e. by differences in patients' environment (community versus psychiatric ward) or in the stage of illness of samples examined (early course versus chronic population in stable phase). Indeed, the current results also echo previous findings from our research group regarding the relationship between QOL and negative symptoms in stable schizophrenia (Rocca et al., 2009a, Rocca et al., 2009b and Rocca et al., 2010a). In a previous work (Rocca et al., 2009a), we found that after the 6 years-course of illness, negative symptoms remain the most reliable predictors of QOL, together with severity of illness, while positive and depressive symptoms have a minor role. Particularly, negative symptoms predominate the influence on QOL yet after the 3-year course of the illness. It is possible that dealing with negative symptoms for such a long time may have a greater impact on QOL than dealing with them for less time. The mean duration of illness (\pm S.D.) in our sample (16.8 ± 11.1 years) can help explain why negative symptoms contribute significantly to QOL.

Second, we explored the specific load of insight and coping in explaining QOL. As for insight, two main results emerged from our work: first, attribution has a direct and positive association with QLS-IF, predicting higher levels of QLS-IF in patients that attribute correctly their symptoms to the illness; second, patients high in negative symptoms are less likely to use attribution. Our study's findings are in line with the results of studies showing a relation between insight and observer-rated QOL (Dickerson et al., 1997, Schwartz, 1998, Hasson-Ohayon et al., 2006, Rocca et al., 2010b, Aghababian et al., 2011 and Kurtz and Tolman, 2011) and in contrast with the results of other studies demonstrating an inverse relationship between insight and subjective QOL (Ritsner, 2003, Sim et al., 2004, Hasson-Ohayon et al., 2006 and Boyer et al., 2012). The complexity among these findings, and in this area of research in general, may be attributed, at least in part, to differences in patient samples (groups of patients in different phases of illness, inclusion of patients with diagnosis other than schizophrenia spectrum disorders), to methodological differences among studies, and likely reflects a number of moderating variables or potential confounding factors. Moreover, due to the complex and multidimensional nature of both insight and QOL, there may not be a simple yes or no answer to the question of the direction of the relation between these two sets of phenomena, which can appear paradoxical (Hasson-Ohayon et al., 2006). Depending on which dimensions of insight and QOL are looked at, insight could have serious costs as well as benefits. The difference between the two constructs "awareness of symptoms" and "attribution of symptoms" might explain previous mixed findings about the influence of insight on QOL. Having poor insight could not always be maladaptive. "Awareness of symptoms" represents the ability to recognize that a particular experience is strange or unusual, whereas "attribution of symptoms" requires the capacity to interpret this experience as a symptom, caused by a disease. On the basis of our results we can hypothesize that the ability to attribute symptoms to illness, requiring the capacity to refer correctly to a situation and to understand the true nature of a condition, can ameliorate indirectly QOL inducing patients to develop personal care skills that mitigate or reduce these symptoms and also to apply adapted skills necessary for

everyday-life, i.e. constructive strategies to face the situation, like seeking help, taking drugs and following rehabilitation programs (Boyer et al., 2012). People with better attribution could be more prone to discuss their mental health problems with others and they also could be more likely to seek support for it; thus enabling success across a variety of domains of QOL (Dolder et al., 2003 and Cooke et al., 2007). Thus, insight can be empowering if it gives the patient a sense of control and enhances compliance with treatment. However, if having insight means accepting the negative attitudes and stigma associated with the diagnosis, it can lead to sense of helplessness and decreased motivation in improving one's status (Hasson-Ohayon et al., 2006). As for the relationship between negative symptoms and insight, studies that have examined the correlations between insight and negative symptoms (Kemp and Lambert, 1995 and Moore et al., 1999; Sevy et al., 2004; Simon et al., 2006 and Monteiro et al., 2008) have often shown conflicting results: some works do not find a correlation (Kemp and Lambert, 1995; Sevy et al., 2004; Monteiro et al., 2008 and Osatuke et al., 2008) while others have shown statistically significant correlations (Moore et al., 1999, Simon et al., 2006 and Osatuke et al., 2008). Negative symptoms are defined as pathological deficits, for example, in thought and adaptive behavior. An etiological theory that considers lack of insight as a negative symptom explains it as "mental withdrawal" from attempting to understand one's own phenomenological experience of the world (Fenton et al., 1997). We can suppose that the severity of negative symptoms can increase patients' difficulty in distinguishing their own subjectivity with respect to the surrounding reality, to recognize a disorder as belonging to their own person and to have awareness of the disorder.

Regarding the issue of coping, two main results emerged from our work: first, social diversion (i.e. the coping strategy oriented to social support seeking) had a direct and positive association with QLS-IF, predicting higher levels of QLS-IF; second, patients higher in negative symptoms were less likely to use social diversion. Avoidance-oriented coping describes activities and cognitive changes aimed at alleviating stress. Social support acts as an important resource and a moderator of coping activities providing opportunities for diversion activities and escape from a problem by seeking out other people. Being with other people may be a way to avoid one's problems. Our findings on schizophrenia outpatients are greatly in line with the results of a cross-sectional study on 161 schizophrenia inpatients (Ritsner et al., 2003), showing that social diversion accounted for 12% of the variance in perceived QOL in schizophrenia inpatients. Thus, social diversion may be considered adaptive, even if it has been suggested that the type or amount of coping that is most adaptive for schizophrenia patients may depend on personal physiological characteristics and that there is neither coping style, nor amount of coping effort, that is best for all (Brenner et al., 2011). As for the relationship between negative symptoms and coping Lysaker et al. (2005) found that individuals with higher levels of negative symptoms are more likely to be resigned to their experiences (i.e. choose not to act because of a perception that nothing can be done), our results suggest the possibility that individuals with negative symptoms feel unable to cope with stress, so they ignore their problems. As they feel unable to cope, it can be expected they worry about their daily activities and develop a tendency to see social situations as opportunities for embarrassment. However, these possibilities must be taken as speculations for future research and certainly rival hypotheses cannot be ruled out including the possibility that other factors not measured contributed to the observed relationships.

Third, although evidence for full mediation to negative symptoms–QLS relationship by attribution and social diversion was not supported in this study, results do suggest that attribution and social diversion partially mediate this relationship. The mediation effects may be interpreted as follows: the use of attribution when dealing with negative symptoms may partially prevent worsening of the QLS. The same outcome for a patient with negative symptoms may be achieved by the utilization of social diversion. Therefore, the mediation models accentuate the patients' active and crucial role in mediating the relationship between the illness and outcome. It is striking that task coping did not emerge as a mediator while social diversion did. As previously proved (Parker and Endler, 1992), task coping is most effective when situations are manageable. When one faces unchangeable

situations, task coping becomes ineffective and emotion or avoidance coping may be the most effective option. That may explain why social diversion, but not task-oriented coping emerges in our sample experiencing symptoms as uncontrollable situations. In the study of Ritsner et al. (2003) distraction coping was found to mediate between paranoid symptoms and subjective QOL in hospitalized patients. Instead, in our study social diversion was found to mediate between negative symptoms and an observer-rated QOL. Whereas in the Ritsner's sample the highly disorganized and transient states that emerge during acute exacerbations are the most upsetting symptoms, we can suppose that in our sample negative symptoms are the most distressing ones, since they reflect enduring clinical traits associated with long-term functional status.

This study has some strengths that should be noticed. First, our sample was relatively large and thoroughly characterized (homogenous with regard to stage of illness and treatment setting, clinically stable outpatients). Among the methodological problems in this area of research Green et al. (2000) pointed out small group size of several studies, heterogeneity in diagnosis and inclusion of mixed groups of inpatients and outpatients. Second, all patients were diagnosed using a structured clinical interview (SCID) rather than clinical charts review. Third, we included in our study only patients with a diagnosis of schizophrenia rather than various psychotic disorders. Fourth, the type of analysis conducted allowed us to explore possible moderators of the effect of negative symptoms on QOL.

However, a number of factors limit the conclusions that may be drawn from this study. First, the data presented are cross-sectional and are unable to address such questions as the evolution of relationships between these domains over time. Second, as is true of most prospective clinical studies that rely on subject recruitment, the studies on which this analysis was based involved sets of inclusion and exclusion criteria. Thus, the study sample may not reflect the full scope of patients who may be encountered in the clinic, leaving open the possibility that the results of this analysis are not fully generalizable to the entire population of patients with schizophrenia. Our study was conducted in a stable, homogeneous community sample that was reflective of baseline levels of functioning and impairment. This point was particularly important due to the fact that there are systematic differences in how QOL interacts with psychiatric symptoms among mixed samples of inpatients and outpatients or early course and chronic patients, and ignoring these differences would obscure results (Eack and Newhill, 2007). Moreover, the literature suggests that symptoms play a more prominent role in patients' levels of functioning as they stabilize after an acute episode (Goldman et al., 1993) or if they reside in community settings and thus have higher levels of functioning (Johnstone et al., 1990, Addington and Addington, 1999 and Norman et al., 1999). However, our results may not be applicable to schizophrenia patients with different clinical conditions, i.e. inpatient or substance-abusing samples. Third, when measuring coping, we measured only the larger style of coping not the specific ways one has coped with schizophrenia. Thus, it remains possible that people cope with mental illness in a manner distinctly different from how they cope in general, though notably, there is no evidence that this is the case. Finally, in the discussion of our findings, we need to consider the possible limitations of the instrument chosen to explore QOL. First, since the QLS was initially devised as a measure of the schizophrenic deficit syndrome, it has been suggested that apathy and other negative symptoms have substantial theoretical overlap with certain constructs tapped by the QLS. Thus, we used a newly constructed modification of the PANSS negative syndrome scale that eliminated items most directly overlapping with measures of community functioning, so as to avoid artificial inflation of the association of negative symptoms and functioning. Second, QLS is an observer-rated instrument. An alternative, or complementary, approach would be to assess functioning through patient self-report of subjective QOL. Indeed, it was reported that in patients with schizophrenia, the subjective rating of QOL may be valid and informative on the point of life satisfaction (Jung et al., 2010). Hence, future study aiming to further explore this issue of determinants of subjective and observer-rated QOL will be needed in schizophrenia patients.

Despite these limitations, this study conducted in a relatively large sample with the same ethnicity representative of the usual setting and modality of care of psychiatric section in a geographically well-

defined catchment area in Italy demonstrated clearly that (a) negative symptoms, attribution and social diversion accounted for 45.3% of the variance of the QLS-IF score in our sample; (b) higher negative symptoms predicted a worse QLS-IF score; (c) social diversion and attribution had a direct and positive association with QLS-IF, suggesting that their use predicted higher levels of QLS-IF; (d) patients high in negative symptoms were less likely to use social diversion and attribution; and (e) attribution and social diversion acted as partial mediators in the negative symptoms–QOL relationship.

5. Conclusions

With replication, along with more research with broader samples, including persons who refuse services and longitudinal designs, these findings could have important implications for clinical practice. As no treatment appears substantially to improve negative symptoms narrowly defined, a greater attention must be given to the presence of attribution and social diversion that may serve to buffer levels of QOL for individuals with higher negative symptoms. These factors are potentially modifiable from specific therapeutic interventions, which can produce considerable improvements in the QOL of this population. These data point to the potential for rehabilitation to include adjunctive treatments that address: (a) social skills training, which has shown potential in ameliorating negative symptoms (Kopelowicz et al., 1997 and McGurk et al., 2007); (b) psycho-educational programs that seek to improve insight, and (c) intervention and rehabilitation strategies focusing on the strengthening of individual coping strategies or teaching new ones with regard to specific symptoms through cognitive, behavioral and psychotherapeutic interventions (Lysaker and France, 1999).

Declaration of interest

None.

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