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.

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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; Rocca et al., 2005), while other studies have identified only a small to moderate relationship (Sim et al., 2004; 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; 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; 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,

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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 ≤ 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