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Dimensional symptom severity and global cognitive function predict subjective quality of life in patients with schizophrenia and healthy adults

Pamela DeRosse^{a,b,c,*}, George C. Nitzburg^{b,c,d}, Melanie Blair^{b,c,e}, Anil K. Malhotra^{a,b,c}

^a Hofstra-Northwell School of Medicine, Department of Psychiatry, Hempstead, NY, USA

^b Center for Psychiatric Neuroscience, The Feinstein Institute for Medical Research, Manhasset, NY, USA

^c Division of Psychiatry Research, The Zucker Hillside Hospital, Division of Northwell Health, Glen Oaks, NY, USA

^d Teachers College, Columbia University, New York, NY, USA

^e Graduate Center, City University of New York, New York, NY, USA

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ABSTRACT

Over the last several decades Quality of Life (QoL) has become increasingly important as an indicator of treatment outcomes; particularly in schizophrenia spectrum disorders because of its close association with functional disability. Numerous studies seeking to elucidate the factors that contribute to QoL in this population have implicated both symptom severity and cognition in determining QoL but the findings have been mixed. The critical factors that appear to impede the lack of consensus in the extant literature examining determinants of QoL include the heterogeneity of the samples and measures examined as well as medication effects across different studies. Thus, the present study sought to address some of these issues by examining the relationship between subjective QoL and both symptom severity and cognitive function in a relatively homogeneous patient sample of patients and a community control sample assessed for dimensional symptom severity. Our results suggest that both global cognitive function and psychiatric symptoms have a significant impact on the subjective QoL of both people with schizophrenia spectrum disorders and psychiatrically healthy adults. Specifically, we found that a global index of cognition as well as self-reported avolitional and depressive symptoms were significantly predictive of QoL in both samples. These findings highlight the importance of addressing cognitive, depressive and avolitional symptoms in the treatment of patients with schizophrenia spectrum disorders and suggest that improvements in these domains may have a meaningful impact on their overall QoL.

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1. Introduction

Quality of Life (QoL) is a multidimensional construct encompassing an individual's perception of their position in life in relation to their culture, goals, expectations, standards and concerns (WHOQOL-Group, 1995). Over the last several decades QoL has become increasingly important as an indicator of treatment outcomes over a wide range of health and disease states. This interest in QoL as an outcome measure has been particularly pronounced in schizophrenia spectrum disorders (SZ) because of its close association with functional disability; a critical problem for patients with these disorders (Lieberman et al., 2008; Malla and Payne, 2005).

To date, numerous studies of people with SZ have implicated general psychopathology such as anxiety and depressive symptoms (Dickerson

et al., 1998; Huppert et al., 2001; Narvaez et al., 2008; Reine et al., 2003) as well as the more specific domains of positive and negative symptoms (Fitzgerald et al., 2001; Norman et al., 2000; Savill et al., 2016) in determining QoL. A recent meta-analysis (Eack and Newhill, 2007) examining the relative contribution of psychiatric symptoms to QoL found that these symptoms have a significant, but small, negative relationship with QoL in patients with SZ. However, these authors acknowledged that their results were limited by the heterogeneity among the samples included noting that sample characteristics such as treatment setting (inpatient vs. outpatient) and illness stage (first-episode vs. chronic), which were commonly intermixed in a given sample, had systematic effects on the observed interaction between QoL and psychiatric symptoms. Thus, they argued that a more concise understanding of the relationship between QoL and symptoms would require the study of more homogeneous samples.

Numerous studies have also implicated cognitive functioning in variation in QoL among patients with SZ, although these studies have also produced conflicting results. While some studies have found positive

* Correspondence to: P. DeRosse, The Zucker Hillside Hospital, Northwell Health, 75-59 263rd Street, Glen Oaks, NY 11004, USA.

E-mail address: pderosse@northwell.edu (P. DeRosse).

relationships (Savilla et al., 2008; Ritsner, 2007; Alptekin et al., 2005; Herman, 2004) others have found negative relationships (Brekke et al., 2001; Dickerson et al., 1998; Narvaez et al., 2008) and yet others have found no relationship (Brissos et al., 2008; Chino et al., 2009; Hofer et al., 2005; Smith et al., 1999). Similar to the findings examining the relation between QoL and symptoms, however, data derived from a recent meta-analysis of the relation between QoL and cognition (Tolman and Kurtz, 2012) also suggests that methodological differences are likely hindering consensus about the nature of the relationship. This meta-analysis indicated that cognition had a moderate effect on measures of *objective* QoL, which is typically clinician rated, but no effect on *subjective* QoL, which is typically self-reported. However, similar to the prior meta-analysis on the relation between symptoms and QoL, Tolman and Kurtz (2012) concluded that the intermixing of samples with different clinical characteristics was likely impacting this latter finding, which was found to be statistically unstable.

One critical issue that was not addressed by either of the aforementioned meta-analyses was the specific way in which subjective QoL was measured. Although both studies differentiated between objective and subjective QoL, a critical distinction given that they are only modestly correlated (Sainfort et al., 1996; Kusel et al., 2007; Bengtsson-Tops et al., 2005), they did not differentiate between general and population-specific measures of subjective QoL. For example, subjective QoL in patients with SZ is commonly measured using the Quality of Life Interview (Lehman, 1988), which was specifically designed for people with serious mental illness and thus, assesses what is deemed clinically relevant in this population and is not typically viewed as valid for measuring QoL in non-psychiatric populations. More recent studies however, have begun to employ more general scales such as the World Health Organization Quality of Life Assessment (WHOQOL) that are valid in both patient and healthy samples. These more general scales appear to be less sensitive to variations in the characteristics of a specific illness such as SZ (Örsel et al., 2004) and thus, may reflect a more comprehensive assessment of QoL. In both aforementioned meta-analyses, studies using both population-specific and general measures of QoL were examined collectively resulting in perhaps an even more turbid understanding of the relation between clinical factors and subjective QoL.

Notably, prior work has also found that antipsychotic medications, which have a wide range of effects on both symptoms and cognitive function as well as a range of adverse effects, also contribute to variation in QoL in SZ patients. For example, Ritsner et al. (2004) found that in a group of patients whose symptoms were stabilized on an antipsychotic medication, those patients who were experiencing adverse events reported significantly lower QoL than those who were not experiencing adverse events. Moreover, a recent randomized controlled trial found that patients taking second generation antipsychotic medications experienced a significantly greater improvement in subjective QoL than those taking first generation agents; an effect that the authors partially attributed to fewer adverse events. Thus, the study of an unmedicated sample examined in parallel to the medicated patient sample might lead to a better understanding of how both symptom severity and cognitive function relate to subjective QoL.

In addition to these methodological complications, recent work has stressed the need for a more dimensional view of the negative symptom construct. Factor analytic studies have consistently demonstrated that negative symptoms can be separated into two broad dimensions: a motivational dimension consisting of avolition, anhedonia and asociality and an expressivity dimension consisting of blunted affect and alogia (Blanchard and Cohen, 2006; Kirkpatrick et al., 2006; Kring et al., 2013). While both of these dimensions may be critical to functional outcomes, data suggests that deficits in the motivational dimension have the greatest effects on functional disability. For example Foussias et al. (2009) found that motivational deficits accounted for 74% of the variance in functional disability in SZ patients, with no additional contribution of deficits in expressivity. Notably, the only study to date that has sought to assess the differential contribution of dimensional measures

of negative symptoms to patients' subjective QoL found that QoL was exclusively related to motivational deficits (Savill et al., 2016). Thus, given the relationship between functional disability and QoL, examination of the role of these two facets of negative symptoms as determinants of QoL seems timely.

The present study aimed to examine the relationship between subjective QoL and both symptom severity and neurocognitive function in 2 distinct samples that varied across a spectrum of symptom severity including a general population sample and a patient sample. Our approach allowed us to address several of the limitations of previous studies. Most notably, in an effort to address limitations of previous work involving the intermixing of sample characteristics including early vs. chronic illness and inpatient vs. outpatient treatment setting, we examined a relatively homogenous group of chronic patients with SZ being treated in an outpatient setting for at least six months. Given that subjective QoL represents how a person feels about their "position in life", we believe that this latter criterion is critical. Patients who are, or were in the recent past, hospitalized at the time of assessment not only have limited control over their daily lives, but they are also unlikely to feel positive about it. Additionally, to address concerns related to the effects of medication status, we examined these relationships using identical measures in a sample of community controls who did not have a psychiatric diagnosis and were not taking any psychotropic medication. Finally, to address the specific effects of different dimensions of negative symptom on QoL, measures encompassing both the motivational and expressivity dimensions were examined.

2. Method

2.1. Participants

The sample was comprised of 149 chronic, stable outpatients with schizophrenia or schizoaffective disorder (95 males, 54 females; $M_{\text{Illness Duration}} = 14.42 \pm 4.86$ years) and 408 healthy adult volunteers (133 males, 275 females). Patient participants were recruited from the Zucker Hillside Hospital (ZHH), a division of Northwell Health, for an NIMH-funded study on functional outcome in schizophrenia (MH079800 to AKM). Patient participants were excluded from the study if they had a psychiatric hospitalization within the preceding 6 months, met diagnostic criteria for current substance abuse (within the past month), or had a history of CNS trauma, neurological disorder or intellectual disability. Healthy volunteers were recruited from the general population via word of mouth, newspaper and internet advertisements and posted flyers for an NIMH-funded study of subclinical psychopathology (MH086756 to PD). Healthy participants were excluded from the study if they had an Axis I affective or psychotic disorder diagnosis, active or recent substance abuse (as determined by urine toxicology) or any disorder known to affect the brain. The patient and control samples used in the present study represent subsets of larger samples and were selected based on the availability of data from the self-report measures used in the analyses. The limited availability of the self-report data was due to the late addition of these measurements to the assessment schedules of these studies. All participants provided written informed consent to a protocol approved by the Institutional Review Board of Northwell Health.

2.2. Clinical assessments

2.2.1. Diagnostic interviews

Patient participants were administered the Structured Clinical Interview for the DSM-IV Axis I Disorders, Patient edition (SCID-I/P) (First et al., 1995b) by Ph.D. or Master's level psychometricians. Information obtained from the SCID was supplemented by a review of medical records and interviews with family informants, whenever possible, and compiled into a narrative case summary. Diagnoses were then determined by a consensus among a minimum of three senior

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