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Dimensional Symptom Severity and Global Cognitive Function Predict Subjective Quality of Life in Patients with Schizophrenia and Healthy Adults

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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

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Contributors

Author PD designed the study and conducted all analyses. Authors GN, MB and AKM assisted in the preparation of the manuscript. All authors contributed to and have approved the final manuscript.

Conflicts of Interest

Drs. DeRosse and Nitzburg and Ms. Blair report no competing interests. Dr. Malhotra has served as consultant or speaker for Bristol-Myers Squibb, Astra Zeneca, Vanda Pharmaceuticals and Clinical Data, Inc, and has received research support from Pfizer, Janssen Pharmaceuticals, Bristol-Myers Squibb, and Eli Lilly.

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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.

Keywords

Quality of Life; QoL; cognition; negative symptoms; depression; MCCB

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 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 2005; 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 (Orsel 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 criteria 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 ZHH faculty, after a thorough review of the SCID and the corroborating information comprising the narrative case summary. Healthy participants were initially administered the Structured Clinical Interview for the DSM-IV, Non-Patient edition (SCID-I/NP) (First et al., 1995a) by Ph.D. or Master's level psychometricians. Information obtained from the SCID was compiled into a narrative case summary and absence of pathology was determined by consensus among two senior members of the ZHH faculty.

2.2.2 Assessment of Psychopathology—All participants were assessed using the Community Assessment of Psychic Experiences (CAPE) (Stefanis et al., 2002). The CAPE is a 42-item, self-report questionnaire that measures three dimensions of subclinical psychopathology including positive, negative and depressive symptoms. The CAPE provides scores on each of the three dimensions as well as a total score representing the overall severity of symptoms. The present study sought to assess the differential effects of specific symptom domains on subjective QoL, with a particular focus on negative symptoms. Thus, although we utilized the standard positive and depressive subscale scores we used the more specific negative symptom subscales described by Barragan et al. (2011), which includes subscale scores for social withdrawal, affective flattening and avolition.

Patient participants were also assessed using standard clinician-administered rating scales to assess symptom severity during the week preceding the interview. These scales included the Brief Psychiatric Rating Scale (BPRS-Hillside version) (Woerner et al., 1988), the Scale for the Assessment of Negative Symptoms (SANS-Hillside version) (Robinson et al., 2000) and the 24-item Hamilton Rating Scale for Depression (HRSD-24) (Hamilton, 1967). These assessments were completed the same day as the CAPE. All clinician-administered scales were administered by Ph.D. or Master's level psychometricians. Inter-rater reliability on all measures, assessed annually using gold standard videotaped interviews, was high (all Kappa's > .80).

2.2.3 Assessment of Quality of Life—To assess subjective QoL, we administered the Quality of Life Scale (QOLS) (Burckhardt and Anderson, 2003), a 16-item self-report measure that assesses six conceptual domains of quality of life including: 1) material and physical well-being, 2) relationships with other people, 3) social, community and civic activities, 4) personal development, 5) fulfillment and recreation and 6) independence. The QOLS is a reliable and well-validated instrument for measuring QoL from the perspective of

patients with chronic illness. Critical to the present study, and in contrast to quality of life measures typically used in patients with schizophrenia however, it is also well validated in samples of healthy individuals and has been shown to produce similar scores across different age, sex and racial groups (Burckhardt and Anderson, 2003). The QOLS is scored by adding up the score on each item to yield a total score ranging from 16 to 112 with higher scores indicating a better quality of life.

2.3 Neurocognitive Assessment

To assess neurocognitive functioning, The MATRICS Consensus Cognitive Battery (MCCB) was administered to all participants. The MCCB is comprised of 10 standardized cognitive measures that capture functioning within seven cognitive domains that are most related to psychotic disorders (Nuechterlein et al., 2008). Although the MCCB provides scores on a range of cognitive domains, in the present study we only used the MCCB Composite score, which provides an index of global cognitive ability.

2.4 Statistical Analysis

To examine the contribution of self-rated positive, negative and depressive symptoms to subjective QoL we carried out two multiple linear regressions; one in patients and one in healthy volunteers, which both employed the same structure. We utilized a block-wise approach to determine the amount of variance in subjective QoL that could be accounted for by global cognitive function and self-reported symptom severity above and beyond the effects of sex and age. Thus, a three-block model was employed in which the first block examined only the effects of age and sex on QoL, the second block included the Composite Score derived from the MCCB and the final block included the overall severity of self-reported symptoms including, positive, depressive, and three domains of negative symptoms (social withdrawal, flat affect, avolition).

3. Results

3.1 Demographics

Comparison of demographic characteristics between patients and healthy volunteers revealed significant differences in the distributions of males and females as well as the distribution of racial groups. Specifically, the group of healthy volunteers had a significantly higher proportion of females and fewer minorities than the patient group. These data are shown in Table 1. Consistent with our prior results (DeRosse et al., 2014b), scores on the CAPE were not normally distributed for either patients or healthy volunteers and thus, comparisons on these measures were carried out using Mann-Whitney U tests. QOLS as well as MCCB Composite scores were normally distributed in both groups and comparisons were conducted using t-tests. As expected, patients scored significantly higher on all CAPE subscales, lower on MCCB Composite score and lower on the QOLS. These results are also shown in Table 1.

3.2 Healthy Volunteers

In healthy volunteers, the full regression model accounted for 31% of the variance in QOLS scores (R^2=0.31; ($F_{(8, 119)}$=7.72, p<.001). The final block of the model, which assessed the

effects of self-reported symptoms above and beyond sex, age and MCCB Composite score, demonstrated a significant increase in the variance previously accounted for by age, sex and MCCB Composite alone (R^2 change =0.34; $F_{(5, 111)}$=11.78, p<.001). In the final model, the specific predictors included MCCB Composite score, self-reported positive symptoms, self-reported depressive symptoms, self-reported social withdrawal and self-reported avolitional symptoms. These results are shown in Table 2.

3.3 Patients

Similarly, the full regression model in patients accounted for 27% of the variance in QOLS scores (R^2=0.27; ($F_{(8, 112)}$=6.47, p<.001) and the final block of the model demonstrated a significant increase in the variance previously accounted for by age, sex and MCCB Composite alone (R^2 change =0.21; $F_{(5, 112)}$=6.86, p<.001). The final model in patients indicated that the specific predictors of QOLS level included MCCB Composite score, self-reported depressive symptoms and self-reported avolitional symptoms. These results are shown in Table 2. Additionally, Figure 1 illustrates the relationship we observed between those predictors of QOLS scores that overlapped in both the patient and healthy volunteer samples.

Although we have previously demonstrated that patients self-reported symptoms are significantly correlated with scores on clinician administered assessments of the same symptom constructs (DeRosse et al., 2014b), it is not clear if scores derived from clinician-administered symptom assessments will relate to subjective QoL in the same way as self-reported symptoms. Thus, to address this question, we repeated the primary regression analysis in patients using the HRSD-24 total score in place of the CAPE depressive symptom score, the BPRS Psychosis Factor score in place of CAPE positive symptoms and the Global SANS scores for affective flattening, avolition and anhedonia in place of the CAPE negative symptom subscales. The results of this analysis were similar to, although not entirely consistent with, the results using self-reported measures of symptom severity. Notably, although we found that the final model using clinician-assessed symptoms was also significant and accounted for 25% of the variance in QOLS scores (R^2=0.25; ($F_{(8, 111)}$=5.63, p<.001) the specific predictors only included age, MCCB Composite score and HRSD Total score; clinician-assessed symptoms of avolition in this model were not significantly predictive of QOLS scores. These results are shown in Table 2.

4. Discussion

The results of the present study 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 of our samples. These findings are generally consistent with prior work in patients indicating that depressive symptoms (Dickerson et al., 1998; Huppert et al., 2001; Narvaez et al., 2008; Reine et al., 2003) and motivational deficits (Fitzgerald et al., 2001; Norman et al., 2000; Savill et al., 2016) are among the strongest predictors of subjective QoL. Moreover, the consistency in the pattern of results relating

depressive and avolitional symptoms to subjective QoL across both groups suggest that these effects are not attributable to medication effects as none of the community controls in the present sample were taking psychotropic medications. Finally, at a general level, the similar pattern observed in both patient and control samples are consistent with the contemporary view of psychopathology, including psychotic experiences, as dimensional rather than dichotomous constructs (van Os, 2010).

Examined independently, the findings in the control sample suggest that while subclinical avolitional symptoms are the strongest predictors of QoL, virtually all domains of subclinical symptoms are predictive of QoL in this population. Although this finding is consistent with prior work in this population (Cohen & Davis, 2009), it is somewhat surprising in that it is not consistent with what we observed in the patient sample. However, it is likely that the discrepant findings are due less to differences in the actual relationships and more to our statistical power to detect them. Table 2 clearly indicates similar relationships in both samples and given the 2.5 fold increase in the control sample (N=408) relative to the patient sample (N=149), this interpretation is likely. Thus, additional work with larger patient samples is needed.

Surprisingly, although we found that global cognitive function was significantly associated with subjective QoL in both patient and healthy volunteer groups, the direction of this relationship differed between groups. In healthy volunteers *lower* global cognitive function, whereas in patients, *higher* global cognitive function, predicted a significantly worse subjective QoL. Given prior work in this area suggesting a positive relationship between cognitive function and QoL (Alptekin et al., 2005; Ritsner, 2007) as well as the substantial literature linking better cognition to better longitudinal outcomes (Green et al., 2004) our finding was unexpected. However, there are several reports in the literature that are directly consistent with our finding (Hofer et al., 2005; Narvaez et al., 2008) and in retrospect, this relationship may be somewhat intuitive. Specifically, patients with relatively intact cognitive functioning may be more likely to feel that they are not reaching their full potential and thus, assess their QoL as being poorer. This is consistent with work by Bowie and colleagues (2007) which found that patients with better cognitive abilities tend to overestimate their level of disability.

Finally, we found that in the patient sample, although clinician assessed depressive symptoms were associated with subjective QoL, consistent with what was found for self-reported depression, clinician assessed avolitional symptoms were not associated with QoL in the same way as self-reported avolitional symptoms. This finding suggests that clinicians and patients may differ in how they view avolitional symptoms. It is likely that this discrepancy, at least in part, is related to the specific scales used in the present study. However, it may also reflect fundamental differences between the objective narrative clinicians have, and the subjective narratives that patients have about psychiatric symptoms. Indeed, although some data suggests that severely ill patients are unable to accurately report negative symptoms (Hamera et al., 1996; Selten et al., 2000), more recent studies have suggested that self-report measures may be both valid and useful in this patient population (Dollfus et al., 2016), especially in the assessment of treatment outcome and overall QoL (Fleischhacker et al., 2005; Lindstrom et al., 2001; Ohata et al., 2014). Thus, the present

findings may add to a growing literature emphasizing the utility of self-reported symptoms in assessing patient-centered outcomes.

Several limitations of the present study should be noted. First, although the CAPE can be scored to produce subscale scores that reflect a dimensional assessment of negative symptoms, it was not specifically designed for this purpose. It should be noted, however, that the negative symptom subscale scores derived from the CAPE were highly correlated with their clinician-rated counterparts (all rho's > .60; all p's <.01). Nevertheless, future efforts seeking to examine the effects of different dimensions of negative symptoms on QoL should utilize more comprehensive measures of these constructs. Additionally, our analyses did not examine the effects of variation within the different cognitive domains assessed by the MCCB but rather, only examined the composite score as an index of global cognitive function. Given our patient sample size, however, the inclusion of all 7 domains captured by the MCCB in our analyses would have substantially reduced our power to detect any meaningful effects. Thus, using the composite score represented a compromise that allowed us to maintain adequate power while still addressing the more global contribution of cognitive function to QoL.

Despite these limitations, the results of the present study have several important implications. First, they suggest that even at subclinical levels, depressive and avolitional symptoms have a meaningful impact on the overall subjective QoL of those experiencing them. Second, these results complement recent work which finds an overlap in the risk factors associated with the development of both clinically-significant and subclinical symptoms (Linscott and van Os, 2013) and supports other work suggesting that they may also have similar consequences (DeRosse et al., 2014a; DeRosse et al., 2014b). These findings highlight the importance of addressing depressive and avolitional symptoms in the treatment of patients with schizophrenia spectrum disorders and suggest that improvements in these symptom domains may have a meaningful impact on their overall QoL. Finally, these findings collectively highlight the need for the type of approach championed by the Research Domain Criteria (RDoC) which calls for the recognition that most clinical problems cut across conventional diagnostic boundaries and exist along a dimension from healthy to various levels of pathological.

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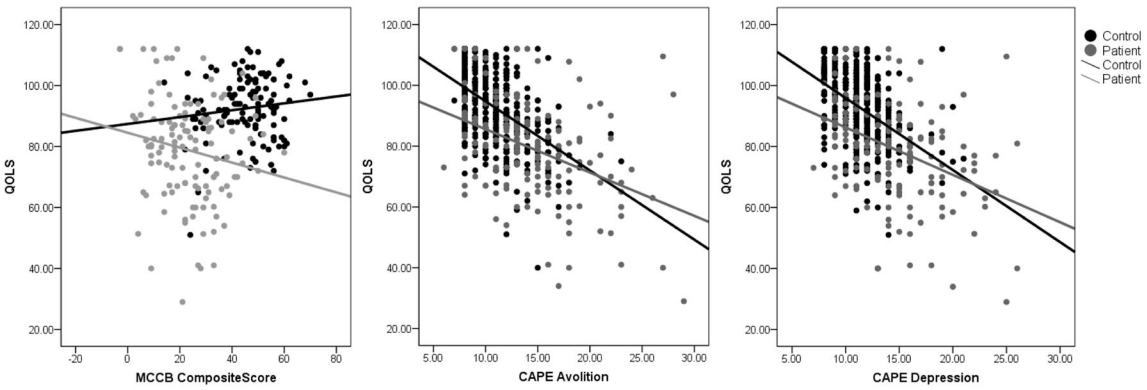

Figure 1.

Simple scatterplots illustrating the relationship between: ***a)*** global cognitive function as measured by the MCCB Composite score ***b)*** self-reported avolitional symptoms and ***c)*** self-reported depressive symptoms (y-axes) and subjective Quality of Life (x-axes) in patients with schizophrenia or schizoaffective disorder (N=149) and healthy volunteers (N=408). *Abbreviations: QOLS: Quality of Life Scale (*Burckhardt & Anderson, 2003*); CAPE: Community Assessment of Psychic Experiences (*Stefanis et al., 2002*); MCCB: MATRICS Consensus Cognitive Battery (Neuchterlein et al., 2004)*

Table 1

Descriptive statistics and comparisons between the patients and healthy volunteers assessed in the present study.

	Patient (N=149)	Control (N+408)	Statistic	p value
Mean Age (SD)	40.61 (11.65)	39.50 (16.73)	t=0.75	***0.45***
Percent Female	36.24	67.4	$\chi 2$=43.83	***<.001***
Race			$\chi 2$=17.86	
White	67	257		
Black	61	61		
Other	21	55		
Mean QOLS (SD)				
Total Score	79.20 (16.82)	92.95 (11.86)	t=9.18	***<.001***
Mean CAPE (SD)				
Positive	32.25 (10.14)	23.35 (3.51)	U=49,956	***<.001***
Depressive	14.53 (4.26)	11.25 (2.20)	U=45,145	***<.001***
Social Withrawal	5.15 (1.73)	4.00 (1.23)	U=43,033	***<.001***
Flat Affect	4.88 (2.01)	3.53 (0.93)	U=43,222	***<.001***
Avolition	14.47 (4.81)	10.78 (2.56)	U=45,202	***<.001***
Mean Clinician-based (SD)				
BPRS Psychosis	5.83 (2.85)	n/a	n/a	n/a
HRSD-24	12.8 (7.34)	n/a	n/a	n/a
SANS Global Asociality/Anhedonia	2.17 (1.13)	n/a	n/a	n/a
SANS Global Affective Flattening	1.85 (1.26)	n/a	n/a	n/a
SANS Global Avolition	2.50 (1.12)	n/a	n/a	n/a

Table 2

Regression results for healthy volunteers (top) and patients (middle) in which models included self-reported symptoms. The bottom segment of the table presents the regression results for the same set of patients in which the model replaced self-reported symptoms with clinician assessed symptoms.

Final Model	***Variable***	**β**	***t***	***p value***
Controls	Age	0.002	0.03	0.976
	Sex	0.08	0.98	0.33
	MCCB Composite	0.12	2.42	*0.02*
	CAPE Positive	0.19	2.02	*0.05*
	CAPE Depressive	−0.26	2.44	*0.02*
	CAPE Social Withdrawal	−0.18	1.99	*0.05*
	CAPE Flattened Affect	0.14	1.46	0.15
	CAPE Avolition	−0.42	3.46	*0.001*
Patients Self-Report	Age	−0.14	1.73	0.09
	Sex	0.02	0.28	0.78
	MCCB Composite	−0.17	2.02	*0.05*
	CAPE Positive	0.08	0.83	0.41
	CAPE Depressive	−3.27	−2.6	*0.01*
	CAPE Social Withdrawal	0.12	1.13	0.26
	CAPE Flattened Affect	0.01	0.08	0.94
	CAPE Avolition	−0.32	2.1	*0.04*
Patients Clinician Assessments	Age	−0.18	2.09	*0.04*
	Sex	0.03	0.34	0.74
	MCCB Composite	−0.28	3.16	*0.002*
	BPRS Psychosis	0.07	0.8	0.42
	HRSD-24	−0.39	4.03	*<.001*
	SANS Global Asociality/Anhedonia	−0.13	1.31	0.19
	SANS Global Affective Flattening	−0.05	0.59	0.55
	SANS Global Avolition	−0.06	0.61	0.54