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Cognitive and symptomatic predictors of functional disability in schizophrenia

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Abstract

Background—Neurocognition and negative symptoms play a major role in predicting functional outcomes in patients with schizophrenia. Few studies have assessed the relationship between functional outcomes and the MATRICS consensus cognition battery (MCCB), which will be central to future clinical trials of cognitive enhancing agents.

Aims—To assess the role of individual MCCB domains on functional outcomes.

Method—185 stable outpatients with schizophrenia were enrolled and assessed with the MCCB, Social Adjustment Scale-II (SAS-II) and Multidimensional Scale for Independent Functioning (MSIF), along with BPRS and SANS.

Results—We found significant relationships between MCCB neurocognitive domain scores, negative symptoms and aspects of functional outcome in schizophrenia. Specifically, we found that work/education functioning is predicted by working memory performance and negative symptoms; residential status (independent living) is predicted by verbal memory scores; and social functioning is predicted by social cognition, attention and negative symptoms. We also found that negative symptom severity was not related to residential status, even though it demonstrated the predicted associations to work and social functioning.

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Conclusion—To our knowledge, this is the first study to assess cognition and functional outcomes using MCCB, SAS II and MSIF. Our results extend prior work and help provide more data on the relationships between cognition, symptoms and functional outcome using “real world” measures.

1. Background

Psychiatric disorders are responsible for an estimated one quarter of the world's disability (Murray and Lopez, 1996). Schizophrenia and schizoaffective disorder (SCZ) together constitute the fifth leading cause of disability (World Health Organisation, 2008) and are responsible for more years of life lived with disability than all malignancies and HIV combined (Harrow et al., 1997; Moller et al., 1988). A functional concept of disability has been defined by the World Health Organisation as “any long-term limitation in activity resulting from a condition or health problem.” Functional disability in SCZ includes a broad range of partially overlapping adaptive impairments (Clinger et al., 1988; Lambert et al., 2006), which collectively lead to substantially reduced quality of life (Heinrichs et al., 1984; Lehman, 1999). The major outcome domains that typically emerge from comprehensive multidimensional outcome scales include: work function, residential status, and social function (Dickerson, 1997; Jaeger et al., 2003; Wallace, 1986).

Although multiple facets of illness may contribute to functional disability in SCZ, neurocognitive function and severity of negative symptoms have been most commonly associated with outcome (Green, 1996; Green et al., 2000; Harvey et al., 2004; McClure et al., 2007; McGurk et al., 2003; Novick et al., 2009; Ojeda et al., 2008; Perlick et al., 2008; Suslow et al., 2000; Ventura et al., 2009). Measures of attention, processing speed, language and memory have been used to predict employment status (Meltzer et al., 1996), impairments in social functioning (Green, 1996), and social skills (Penn et al., 1995), as well as response to training in social and vocational skills and interpersonal problem solving (Addington and Addington, 1999; Bellack et al., 1994; Kern et al., 1992; Lysaker et al., 2005; McGurk and Mueser, 2006; Xiang et al., 2006). Social cognition deficits have also recently been associated with daily and community functioning in schizophrenia (Brekke et al., 2005; Couture et al., 2006; Sergi et al., 2007; Vauth et al., 2004) accounting for a proportion of variance beyond that explained by basic neurocognitive measures e.g. (Brune, 2005; Corrigan and Toomey, 1995; Pijnenborg et al., 2009; Pinkham and Penn, 2006; Roncone et al., 2002).

Although there exists consensus that neurocognition plays an important role in functional outcome in schizophrenia (Green et al., 2004) most studies to date have been limited in scope. For example, 17 studies which included measures of symptoms, neurocognition, and functioning were examined in a recent meta-analysis (Ventura et al., 2009); the median sample size was 66, and none of the studies included measures of all 7 cognitive domains identified by the NIMH MATRICS project (Nuechterlein et al., 2004). Very recently, however, there have been three large-scale studies on the relationship between cognition, symptoms and functional outcome: Bowie et al. (2008) performed comprehensive assessment of 222 older schizophrenia outpatients. Using path analyses, they demonstrated that negative symptoms and multiple neurocognitive domains (attention/working memory, verbal memory, processing speed and executive functioning) had both direct and indirect effects on functional outcome. While the full set of cognitive and symptom predictors accounted for 20%–35% of the variance in outcome measures, individual contributions were generally modest. Similar results, marked by low correlation coefficients and relative lack of specificity, were reported in a path analysis of 395 schizophrenia patients enrolled in a one year treatment trial (Lipkovich et al., 2009), assessing dependent measures derived from the Heinrichs–Carpenter Quality of Life Scale (QoL) (Heinrichs et al., 1984). Finally, Mohamed

et al. (2008) assessed 1,386 patients included in the CATIE clinical trial, also using the QoL. While neurocognitive functioning was assessed across multiple domains (processing speed, working memory, verbal memory, vigilance, and reasoning), only a composite score representing the first principal component (general cognitive ability) was analyzed. Convergent with prior reports, both negative symptoms and the average composite neurocognitive scores were significantly (though modestly) correlated with overall quality of life as assessed by the QoL.

Although these recent studies consistently support the hypothesis that negative symptoms and neurocognition predict social and functional outcome, several caveats should be considered. First, the dependent measures used in the prior studies are dimensional, but prior research suggests that outcomes in patients with schizophrenia are not normally distributed (Harrow et al., 2005); these dimensional scores do not readily translate into clinically relevant outcomes or categories. Moreover, interpretation of modest correlation coefficients across global measures of cognition and function is necessarily equivocal. Second, prior studies have assessed non-representative cohorts, including elderly patients and subjects enrolling in clinical trials, which may be significantly different from patients in the community who are less likely to tolerate long follow up schedules. Third, the outcome measures do not usually account for the level of support needed to attain a given functional status or other unmeasured contributors to function. Fourth, social cognition has not been assessed in these three studies. Finally, these studies did not utilize the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) consensus cognitive battery (MCCB).

There are a number of advantages to adopting the MATRICS Consensus Cognitive Battery (MCCB) (Green et al., 2004) for studies of cognition in schizophrenia. First, each test has been vetted on properties including test-retest reliability, utility as a repeated measure, practicality, and tolerability (Nuechterlein et al., 2008) and it has been administered to 300 community volunteers across five US sites for co-norming and standardization (Kern et al., 2008). Practice effect data on the normative sample are also reported. Second, the MCCB has been translated into eight languages and is being widely implemented in ongoing studies of patients with SCZ internationally, making this battery useful for consistent comparisons across samples worldwide. Finally, the ongoing development of preclinical batteries (Young et al., 2009) that will parallel or complement the existing MCCB, suggests that future translational work will be made easier by inclusion of the MATRICS subtests in current data collections.

Although the MCCB represents an important step in unifying cognitive outcome measures for clinical trials in schizophrenia, there are a number of potential disadvantages or limitations to the battery as well. Although brevity may be seen as a strength, the MCCB only very briefly taps into some of the more broadly defined cognitive domains. For example, there is only a single measure that captures executive functions other than working memory (NAB Mazes) and this is a task that has not been widely used in psychiatric samples. Further, some of the tests chosen are considerably less taxing than alternate measures, such as the HVLT in comparison with the more difficult California Verbal Learning Test (CVLT), which also provides indices of learning strategy not available on the HVLT (Delis et al., 1987). Finally, although the MCCB includes a measure of social cognition (the MSCEIT Managing Emotions), this is undoubtedly a complex construct and a more detailed assessment will be needed to adequately evaluate this domain.

Given the advantages and the disadvantages of the MCCB as an assessment tool in schizophrenia, it remains prudent to include this battery in studies such as ours which focus on functional outcome. Just as the US FDA has recommended the use of the MCCB for

clinical trials of cognitive enhancement in schizophrenia, it has also set forth a requirement for including co-primary measures of everyday function, that will putatively track with changes in MCCB performance. Specifically, for an agent to receive an FDA indication for cognitive enhancement, these co-primary functional outcome measures will need to improve significantly in addition to any cognitive changes detected with the MCCB. Thus, it is of practical importance to evaluate whether performance on the MCCB is significantly associated with everyday functioning in patients with schizophrenia.

To address some of these issues, we have assessed 185 schizophrenia patients from the general community. These patients had been symptomatically stable for six months, represent a representative “real world” sample, and were assessed with a comprehensive array of clinical, neurocognitive, social and functional disability measures. Moreover, we utilized each of the MCCB domain scores, thereby including a measure of social cognition. We used a functional outcome measure, the Multidimensional Scale for Independent Functioning (MSIF), which specifically assesses the contextual influences on functional outcome by independently rating role position, level of support, and role performance in each of three environments: work, education and living (Jaeger et al., 2003). Finally, we dichotomized this outcome measure to more closely approximate outcomes of clinical relevance to patients and their families.

2. Methods

2.1. Subjects

The study was based at the Zucker Hillside Hospital, a division of the North Shore–Long Island Jewish Health System, which serves the mental health needs for approximately five million residents in the New York City area. It provides mental health services for approximately 250,000 outpatient visits, 14,000 inpatient discharges, 65,000 patient days in Partial Hospitalization/Day Treatment, and 10,000 visits in Psychiatric Rehabilitation per year. Moreover, the Hospital has research collaboration with multiple sites in the region, including NeuroBehavioral Research, Inc, from which subjects were also ascertained. An additional site for recruitment was the Manhattan Psychiatric Center, in New York City, which provides comprehensive mental health services to an inner city population with long-term and persistent mental illness. All participating subjects provided written informed consent to a protocol that was approved by the Institutional Review Board at each institution.

A total of 185 stable outpatients between 18 and 59 years of age with a DSM-IV diagnosis of schizophrenia or schizoaffective disorder, with no current substance abuse (within the past 6 months) were recruited between 2007 and 2009. Potential subjects were screened to rule out any history of CNS trauma, neurological disorder (including seizures), mental retardation, or known genetic disorder. Additionally, we excluded any patient with a psychiatric hospitalization within the past 6 months.

2.2. Diagnostic assessment

Each subject was assessed with the Structured Clinical Interview for the DSM-IV (SCID-IV) administered by trained and reliable raters. 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 expert diagnosticians from the ZHH faculty.

2.3. Psychopathology assessment

Patients were also assessed for current symptoms using the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962), the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1983) and the Hamilton Rating Scale for Depression (HRSD-24) (Hamilton, 1960). All psychopathology assessments were completed within 36 h of the cognitive assessment.

2.4. Cognitive assessment

All subjects underwent neurocognitive assessment, which included the MATRICS Consensus Cognitive Battery (MCCB). The MCCB has robust psychometric properties, having been specifically constructed to rapidly yet comprehensively and reliably examine cognitive functioning in patients with schizophrenia (Nuechterlein et al., 2008; Kern et al., 2008). The MCCB evaluates seven domains of cognitive function including: 1) speed of processing using the Brief Assessment of Cognition in Schizophrenia (BACS) and Trail Making Test part A; 2) attention using the Continuous Performance Test—Identical Pairs (CPT-IP); 3) working memory using the Wechsler Memory Scale (spatial and letter-number span); 4) verbal learning using the Hopkins Verbal Learning Test—Revised (HVLT-R); 5) visual learning using the Brief Visuospatial Memory Test—Revised (BVRT-R); 6) reasoning and problem solving using the Neuropsychological Assessment Battery (NAB) Mazes subtest; and 7) social cognition using the Mayer–Salovey–Caruso Emotional Intelligence Test (MSCEIT). The MCCB also produces a composite score, which is derived from the scores on the sub-domains (MCCB Composite). Following common practice in the psychiatric literature (Keefe et al., 2005), we estimated premorbid IQ using the Wide Range Achievement Test-Third Edition-Reading Subtest (WRAT-3). WRAT-3 is a test that assesses single word reading skill which, like command of general knowledge and vocabulary, is particularly resistant to the effects of deterioration associated with brain disease and is considered an estimate of pre-morbid IQ in patient populations (Kremen et al., 2006).

2.5. Functional outcome assessment

To assess functional ability we utilized two primary outcome measures including the Multidimensional Scale for Independent Functioning (MSIF; Jaeger et al., 2003) and Social Adjustment Scale-II (SAS-II; Schooler et al., 1979). These scales were selected based on their ability to comprehensively assess critical aspects of functional outcome, with a particular focus on work function, residential status, and social functioning.

The Multidimensional Scale of Independent Functioning (MSIF) is an anchored scale which measures real world functional performance in three environments: work, education, and independent living (Berns et al., 2007; Jaeger et al., 2003). It captures contextual influences on functioning by independently rating role position, level of support and role performance. For example, within the work environment, role position refers to the actual job role, level of responsibility, full-time versus part-time, etc. Support for work refers to the presence and level of involvement of a job coach or family member, whether the support is on site at all times (as in a work enclave), whether the support provider is a clinician or work supervisor, and whether work is segregated in an agency entirely devoted to disabled workers (as in sheltered work). Global MSIF ratings within each environment are then made which reflect the overall level of functioning in the context of a range of available supports. Scores range from 1 to 7, with higher scores indicating poorer function. The MSIF has been previously validated in psychiatric outpatients predominantly with schizophrenia or schizoaffective disorder and shown to have good criterion, discriminant, interrater, and construct validities (Jaeger et al., 2003).

MSIF ratings are made primarily using information from a semi-structured interview with the patient. External sources of information are also used when available, including clinical charts and interviews of family, employers, rehabilitation and housing counselors, and clinical staff. All ratings receive final scoring following a consensus rating conference led by a study investigator (P.D.). We utilized the global scores for work and residential domains as primary dependent measures. For those subjects whose primary employment status was 'student', we utilized the global educational domain score in place of the work score.

The SAS-II assesses social functioning using a semi-structured interview. Subscales assess work role (including student role), household role, parental role, external family role, conjugal and non-conjugal sexual roles, romantic involvement, social and leisure activities, and personal well-being. We utilized the global Social/leisure rating as the primary dependent measure derived from this scale. Scores range from 1 to 7, with higher scores indicating poorer social ability.

2.6. Statistical analyses

The distribution of scores for each of the three major dependent measures (work/educational functioning and residential status from the MSIF, and social functioning from the SAS-II) significantly deviated from normality (one-sample Kolmogorov-Smirnov tests with Lilliefors significance correction; all p -values $< 10^{-12}$). In addition, the two MSIF scales demonstrated significant negative skew (3–4 times the standard error of the skewness), with a large mode substantially greater (worse functioning) than the mean. Based on these distributions, we opted to use these measures in a dichotomous manner, which we felt would represent more clinically relevant outcome variables. In each case, patients with modal scores were designated as having "poor" outcome, while patients in the tail of the distribution were designated as "good" outcome.

Specifically, patients with a score of 6 or 7 on either Work or Education status (6=part-time, nonmainstream setting, or unemployed/not in school) were categorized as "poor" and those with a score of 5 or less (5=some responsibilities, very part-time but in a mainstream setting) were classified as "good" Work/education status. We combined the ratings derived from the Work and the Education scales, rather than interpreting them independently, thereby capturing subjects who were either students, and perhaps not currently working (most relevant functional score would be for education), or those who were working and not currently enrolled as a student (most relevant functional score would be for employment). For Residential status, we used the clinically relevant cut-off of score of 3 or less (3=mainstream residential environment with full responsibility) to describe those with "good" residential status and those with a score of 4 or greater (4=non-mainstream residential environment or mainstream with less responsibility) as having "poor" residential status. Similarly we defined a score of 3 or less (3=good adjustment) on the SAS-II as having "good" social functioning.

We examined the relationship between the neurocognitive, clinical and functional variables using logistic regression separately for each of the three dichotomized outcome measures (work/education, residential, and social/leisure). As our primary aim was to identify the contribution of specific cognitive domains independent of demographic variables, symptoms, and premorbid cognitive status, we employed a backward stepwise regression model, with forced entry of demographics (race, sex, age) in Block 1 and stepwise conditional entry ($p < 0.10$) for the following variables in three subsequent blocks: Block 2: Total SANS score, Total BPRS score, Total Ham-Dscore; Block 3: WRATscore (estimated premorbid IQ); Block 4: Individual MCCB domain scores.

3. Results

3.1. Demographics and distributions

The mean age of the study participants was 42.8 years $\pm$ 10.1. Nearly half (42%) of the sample was Caucasian, with 9.7% Hispanic, 38.9% African American and the remainder were other minorities including Asian and mixed ethnicities. For purposes of analysis, this variable was dichotomized into Caucasian/non-Caucasian. Sex distribution of participants was 68% male and 32% female. Mean Ham-D score was 10.39 $\pm$ 7.00, mean BPRS score was 31.82 $\pm$ 7.62, mean SANS score was 7.21 $\pm$ 2.34 and the mean SAS score was 4.04 $\pm$ 1.13. A summary of the performance on the MCCB domains is provided in Fig. 1.

Each of our dependent measures was dichotomized as described in the methods section. For each functional domain, one-quarter to one-third of all subjects were rated in the “good” outcome category, consistent with epidemiological studies (Harrow et al., 2005). A summary of combinations of frequencies of subjects on different assessments of function is provided in Table 1. Only 6% of the patients had a good outcome on all measures, whereas 41.4% of the patients did poorly on all scales.

3.2. Specific demographic, clinical, and cognitive predictors of functional outcomes

For the Work/Educational functioning domain, 31.3% of all patients were classified as having good outcome and 68.7% had a poor Work/Educational status (data missing for 3 individuals). In the logistic regression model, work/education status was significantly predicted by the degree of negative symptoms ($p < 0.001$), with working memory contributing significant independent variance ($p = 0.044$ in the final model, and $p = 0.037$ for change in model when the working memory term is removed). Age, sex and ethnicity were not significant predictors of work/education functioning. A summary of demographic predictors and variables significantly entering the model is presented in Table 2.

Dichotomization on residential status resulted in 72.4% ($n = 134$) of our study group being characterized as having poor residential functioning, whereas 27.6% ($n = 51$) had a good residential functioning. In our regression model, we found a significant effect of verbal memory on residential status in the final model ($p = 0.048$), which significantly contributed to the variance after demographic variables, symptom variables and premorbid IQ ($p = 0.045$). Age, sex and ethnicity were not statistically significant predictors of residential status. Additionally, none of the clinical symptom measures remained in the model as significant predictors. A summary of demographic variables and variables found to be significant is presented in Table 3.

For social functioning, 33.7% of our subjects were classified as good outcome compared to 66.3% who had a poor outcome in social functioning (data missing, $n = 1$). Social outcome is predicted in our final logistic regression model by ethnicity ($p = 0.044$), negative symptoms ($p = 0.011$ in the final model; $p = 0.014$ for change if removed), social cognition scores ($p = 0.027/p = 0.023$) and, marginally, attention/vigilance scores ($p = 0.054/p = 0.047$). The regression coefficient for the attention/vigilance score indicated a reverse relationship (better outcome associated with lower attention scores). Age and sex were not significant predictors of social status. A summary of demographic variables and variables significantly entering the model is presented in Table 4.

3.3. Tests of generalized effects

As noted in the introduction, some prior studies have demonstrated a predictive effect of generalized cognitive deficit. We excluded this possibility in our dataset in several ways. First, we tested multicollinearity of the cognitive predictors by examining the correlation

matrix of the MCCB domain scores. These domain scores are only moderately intercorrelated, with mean $r=0.31$ (median $r=0.32$), indicating that, on average, any given test shares ~10% of the variance with any other. Moreover, no test shares more than a third of the variance with any other test. Second, we tested the effects of generalized deficit in the logistic regression models in two ways: 1) WRAT scores failed to significantly enter any of the logistic regressions as shown in Tables 2–4; 2) when the MCCB domain scores are replaced in the logistic regression models by the MCCB composite score, the composite fails to significantly enter any of the three models. Third, we re-ran each logistic regression model with each domain score entered in isolation; no MCCB domain score enters any of the models even at relaxed $p<0.10$ except for those that are reported as significant in the original analyses (Tables 2–4).

4. Discussion

The primary findings of this study indicate a relatively specific set of relationships between MATRICS Consensus Cognitive Battery (MCCB) neurocognitive domain scores and aspects of functional outcome in schizophrenia. We found that: 1) work/education functioning is predicted by working memory; 2) residential status (independent living) is predicted by verbal memory; and 3) social functioning is predicted by social cognition and (marginally) attention. Moreover, we found that negative symptom severity was not significantly related to residential status, even though it demonstrated the predicted associations to work and social functioning.

Prediction of functional impairment in a disease as complex and variable as schizophrenia can be a challenge. Our study utilized assessment tools, MSIF and SAS II, intended to assess “real world” functional disability. The MSIF provides a contextual approach to functional disability in our patient population to provide a better understanding of all facets of the patients' lives. This scale takes into account not only the patients' functioning but the context of support that they receive from their families, the community or the state. Similarly, the SAS II also takes into account the patients' various roles and positions and their subsequent performance. Using these scales and deriving clinically meaningful cutoff values, our study extends prior research utilizing dimensional approaches to measuring outcome. It is interesting to note that the groups rated as “poor” in each of the three dependent variables of social functions are to some extent correlated (Table 1); nevertheless, the MCCB domains contributed differentially to each of the three dependent variables. Combined with the lack of an effect of generalized cognitive deficit, our results suggest that specific functional disability outcomes may be dissociably predicted by domain-specific cognitive performance.

To our knowledge, our study presents the first data to examine the relationship between the MCCB measure of social cognition, the MSCEIT, and real-world social functioning in schizophrenia. These data are consistent with prior work suggesting a relationship between social cognition and social function (for review, see Couture et al., 2006). In general, these studies utilized facial emotion recognition tasks as measures of social cognition. For example, Kee et al. (2003) studied the relationship between functional outcomes and social cognition in 94 clinically stabilized schizophrenic outpatients. Two psychosocial outcome measures (Strauss and Carpenter Outcome Scale and Role Functioning Scale) were used and the Facial Emotion Identification Test Outcome Scale was used to measure social and emotional cognition. Using principal components analysis, they found emotion perception to be significantly associated with work functioning/independent living in their cross-sectional analysis as well as prospectively over the 12 months. Their causal model suggests perception of emotion might cause work functioning/independent living outcome over one year. We attempted to extend their approach by using the component of the MSCEIT

incorporated in the MCCB involving social judgments, which is believed to have greater reliability (Green, 2006) and may have greater ecological validity.

We found the MCCB domain of verbal memory to contribute to residential status. Although they did not have a direct measure of residential status in their study, Bowie et al. (2008) found a similar result such that community activities were predicted by verbal memory. This is in contrast to Verdoux et al. (2002) who evaluated 35 patients for two years and did not find an association between cognitive performance, including verbal memory, and residential outcome. However, Verdoux et al. (2002) examined younger patients (mean age 32), a cohort which may have different demographic and social characteristics than our patient population. Also, the patient population studied by Verdoux et al. consisted of inpatients who were later followed after discharge, while our sample was comprised of patients stable in the community setting.

We also found negative symptoms to be a predictor of social function as well as work-educational status. Negative symptoms have consistently been shown to be one of the major predictors of functional outcome (McClure et al., 2007; McGurk et al., 2003; Novick et al., 2009; Ojeda et al., 2008; Suslow et al., 2000; Ventura et al., 2009). Bowie et al. (Bowie et al., 2008) found that the relationship between the severity of negative symptoms and work skills/community activities was mediated through social competence, an area that was not measured in the present study. These authors showed a direct relationship between negative symptoms and interpersonal behavior. We could not find a relationship between positive symptoms or symptoms of depression with any of the functional outcome indicators. This is in contrast with several recent studies (Bowie et al., 2008; Lipkovich et al., 2009; Mohamed et al., 2008), which have demonstrated a small, albeit statistically significant, association between positive symptom levels and functional domain scores. This discrepancy may be due to several factors. First, the differences in ascertainment may result in different ranges of values, with clinical trials patients having greater levels of positive symptomatology compared to our clinically stable patients (Lipkovich et al., 2009; Mohamed et al., 2008). Second, it is important to emphasize that our study was designed to assess patients at their usual, sustained level of functioning. Patients entering a clinical trial may experience functional decline that is not representative of their full capacity. Third, it is possible that through our use of dichotomized dependent measures, which may be less sensitive to incremental differences, that the role of positive symptoms is not large enough to affect categorical change in functional status. It should, however, be noted that the values for percentage of variance explained by our models (10–18%) was comparable to that presented in the CATIE study (Mohamed et al., 2008), but weaker than the path analytic models presented by Bowie et al. (2008). The maximal R^2 (Nagelkerke) for any of our models was 0.18, nearly half that reported by Bowie et al. (2008).

Several limitations of our study should be noted. First, our study utilized a cross-sectional design, in contrast to some studies which have a prospective design. The cross-sectional design enabled us to recruit a larger number of patients that are sometimes lost to follow up in prospective studies. It does, however, lack the benefits of providing a better illustration of changes over time in subject population. Second, our sample size was lower than Bowie et al. and Mohammed et al. who were recruiting subjects from other, larger studies. Nevertheless, our data is largely consistent with prior findings and may have increased generalizability to the outpatient schizophrenia population. Finally, our dichotomization of the dependent variables may lead to decreased sensitivity overall, but provides the potential advantage of a more clinically meaningful assessment of the subject population.

Our study highlights the importance of both the negative symptoms of schizophrenia and domain-specific deficits in cognition toward the prediction of outcomes in schizophrenia.

Schizophrenia is a complex disorder with deficits that extend to clinical and cognitive domains. This study represents an attempt to measure the real life disability caused by those deficits. This process is still evolving and better measures are needed to adequately capture all aspects of the patient's functional status across diverse clinical populations.

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Fig. 1.
Mean scores and 95% confidence intervals of individual cognitive domains.

Table 1

Combinations of frequencies of subjects on different assessments of function.

Residential Status	Work/Ed status	Social status	Number of patients (out of 181 total)	Percentage
Bad	Bad	Bad	75	41.4
Bad	Bad	Good	18	9.9
Bad	Good	Bad	17	9.4
Bad	Good	Good	20	11
Good	Bad	Bad	19	10.5
Good	Bad	Good	13	7.2
Good	Good	Bad	8	4.4
Good	Good	Good	11	6.0

Table 2

Prediction of Work/Ed Function by basic demographic variables, working memory and SANS score.

	B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I. for EXP(B)		
							Lower	Upper	
Ethnicity	-0.707	0.430	2.697	1	0.101	0.493	0.212	1.146	
Gender	-0.236	0.444	0.282	1	0.596	0.790	0.331	1.888	
Age	-0.016	0.021	0.579	1	0.447	0.984	0.946	1.025	
Total SANS score	-0.274	0.079	12.042	1	0.001	0.760	0.651	0.888	
Working Memory	0.035	0.017	4.060	1	0.044	1.036	1.001	1.072	
Constant	1.271	1.107	1.318	1	0.251	3.566			

Table 3

Prediction of Residential Function by basic demographic variables and verbal learning.

	B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I. for EXP(B)		
							Lower	Upper	
Ethnicity	0.681	0.406	2.811	1	0.094	1.975	0.891	4.378	
Gender	0.502	0.416	1.456	1	0.227	1.652	0.731	3.736	
Age	0.022	0.021	1.077	1	0.299	1.022	0.981	1.064	
Verbal learning	0.050	0.025	3.916	1	0.048	1.051	1.000	1.105	
Constant	-4.646	1.385	11.252	1	0.001	0.010			

Table 4

Prediction of Social function by basic demographic variables, attention, social cognition and SANS score.

	B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I. for EXP(B)	
							Lower	Upper
Ethnicity	0.802	0.398	4.067	1	0.044	2.230	1.023	4.864
Gender	0.024	0.429	0.003	1	0.956	1.024	0.442	2.373
Age	-0.020	0.020	0.980	1	0.322	0.981	0.943	1.019
Sum of SANS score	-0.174	0.068	6.526	1	0.011	0.840	0.735	0.960
Attention	-0.035	0.018	3.708	1	0.054	0.965	0.931	1.001
Social cognition	0.039	0.017	4.894	1	0.027	1.039	1.004	1.076
Constant	0.908	1.231	0.544	1	0.461	2.480		