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Self-awareness of functional impairment in individuals at clinical high-risk for psychosis

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Abstract

Aims—A major public health concern associated with schizophrenia is the long-term disability that involves an inability to function independently in the community. An individual's self-awareness of functional impairment may be a significant factor contributing to long-term disability. In fact, subjective interpretation of one's illness impacts treatment participation and adherence, and is linked to poor outcomes. However, it remains unclear how illness-related functional impairment is perceived by individuals prior to the onset of psychosis. This study aims to examine the relationship between clinician-based and self-report assessments of functioning, as well as the contribution of clinical symptoms to this relationship in individuals at clinical high-risk for psychosis.

Methods—The Sheehan Disability Scale, a self-rated instrument, was used to measure disruption in daily functioning in social and role functioning due to symptoms in a sample of 73 treatment-seeking patients at clinical high-risk for psychosis and 50 healthy controls.

Results—Relative to healthy controls, clinical high-risk patients self-reported significant disruptions in social and role functioning. In addition, a specific relationship emerged in that clinician-rated measures of functioning and depression were related to disability scores.

Conclusions—These findings suggest that clinical high-risk patients are significantly disturbed by their illness. Self-reported disruption of daily functioning was associated with clinician-rated functioning and depressive symptoms, further highlighting the impact of functional impairments on the level of distress experienced by patients in the early phases of the illness. Intervention strategies that repair functional impairment before the onset of psychosis may prevent long-term disability.

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Introduction

Psychiatric disorders are the leading cause of disability in the United States (1), resulting in disability that is comparable to chronic medical conditions (2). In particular, schizophrenia imparts a significant familial, societal and economic burden (3, 4). On an individual level, disability in schizophrenia is often characterized by significant social and role functioning impairments (5, 6). These functional impairments often precede the onset of the disorder, as evidenced in cohort (7, 8), retrospective (9), and genetic high-risk studies (10, 11). Also, more significant functional impairments early in the disorder predict poorer functioning later (12-14). Understanding what factors contribute to poor functioning early on may help lead to better strategies for preventing long term disability in individuals with schizophrenia.

The ideal time to intervene would be prior to the onset of the disorder and at a point where social, academic, and occupational skills are acquired. This typically occurs during adolescence and early adulthood. While several studies have demonstrated that functional impairments are present at the first episode (15, 16), recent findings from prospective clinical high-risk (CHR) studies suggest that impairments in maintaining social/interpersonal relationships and managing academic/occupational tasks are present several years before the first hospital admission (17, 18). In fact, poor social functioning in CHR patients predicts the onset of psychosis in complex prediction models (19, 20), as well as in models specifically tailored to study the relationship between functioning and onset of psychosis (21), indicating that baseline functioning can distinguish those who ultimately develop a psychotic disorder from those who will not. Recent data from Cornblatt et al.(22) indicates that impairments in social and role functioning are stable over time and independent from clinical state, suggesting that rather than specifically predicting psychosis, pre-illness impairments in functioning may be a critical predictor of long-term disability. Moreover, even after remission of the attenuated positive symptoms, individuals at CHR continue to have significant functional deficits (17). Thus, it is clear that functional impairments are pervasive in a CHR sample and they are not necessarily dependent on the presence of attenuated positive symptoms. It is possible that these impairments could persist indefinitely unless they are addressed during this critical period.

Although there is extensive evidence that individuals at CHR have functional impairments (17, 18, 21), little is known about how these functional difficulties are perceived and interpreted by an individual at a heightened clinical risk for psychotic illness. Despite the presence of substantial pre-illness social and academic/occupational difficulties, it is subjective distress that frequently motivates pre-illness treatment seeking (23, 24). However, it remains unclear if subjective assessment of functioning is associated with clinician rated functioning in CHR patients. Clinician-based assessments of social and role functioning are typically determined by facts and achievement in social relationships and academic/occupational performance and do not take into consideration the level of distress experienced by the individual. As a result, there may be a disconnect between the rater's and the subject's interpretation of their functional difficulties.

In fact, it has been well documented that adults with chronic schizophrenia are unaware of the symptoms and general consequences of the disorder (25, 26). For example, Bowie et al.

(26) found that self-report and case manager ratings did not converge in multiple domains of functioning, including interpersonal skills, activities in the community, and work skills. Atkinson et al. (27) reported that individuals with schizophrenia self-reported a good quality of life, although clinician-ratings suggested that they had a great deal of functional impairment. Contrary to this, a study of individuals with first-episode psychosis showed subjective and objective ratings of social/role functioning were highly related (15). Given that subjective reaction to illness may contribute to treatment adherence (28) and functional outcome (29), examining the link between objective and subjective functioning prior to the onset of illness may provide additional information to evaluate the extent that functioning deficits are present and if they have an impact on the individual.

The present study examined whether individuals at CHR for psychosis accurately identify impairment in their social and role activities as a result of their clinical symptoms. The Sheehan Disability Scale was used to assess self-reported interference and disruption in daily social and role functioning caused by current symptoms (30). In addition, clinician-rated social and role (academic/occupational) functioning was assessed with the Global Functioning: Social and Role scales, developed specifically for use with prodromal adolescents and young adults (18). We hypothesized that individuals at CHR would report significant social and role functioning impairments relative to healthy controls using both subjective and objective measures. Based on evidence that individuals with first-episode psychosis patients (but not chronic schizophrenia patients) showed subjective and objective ratings of social/role functioning were highly related, we hypothesized that there would be a strong relationship between self-reported and clinician assessments of functioning in CHR patients. Finally, we measured clinical symptoms, such as attenuated positive symptoms, attenuated negative symptoms, depression and anxiety, in order to determine if clinical symptoms contribute to self-reported ratings of social and role functioning above and beyond clinician-rated functioning. There is some data to suggest that self-rated poor functioning is associated with more severe depressive symptoms (16, 31, 32), but not more severe attenuated positive and negative symptoms (15, 16). Therefore, we expected our model to include depression, but not attenuated positive and negative symptoms, as a significant factor associated with self-reported functional impairment above and beyond clinician-rated functioning.

Methods

Participants

Participants were recruited to the Recognition and Prevention (RAP) Program during Phase I (2000-2006). The RAP Program is a longitudinal research program for adolescents and young adults considered to be at clinical high-risk (CHR) for psychosis. Patients were referred to the program from the outpatient and inpatient services at The Zucker Hillside Hospital, schools, community professionals, and concerned family members. Written, informed consent was obtained from the patient if they were 18 years or older, or from their parent (with patient's written assent) if the patient was under 18 years. The research protocol was approved by the Institutional Review Board at North Shore-Long Island Jewish Health System (NS-LIJHS).

A total of 191 prodromal patients participated in the RAP study in Phase I. Patients were included in the study if they met criteria for one of three CHR categories that were based on scores from the Scale of Prodromal Symptoms (SOPS; 33). This scale is comprised of five positive symptoms, six negative symptoms, and four disorganized and general symptoms that are rated on seven point scale from 0 (absent) to 6 (psychotic/extreme). Patients were classified as CHR Negative (CHR-; N=55) if they had a score of moderate or higher on any negative symptom (and no attenuated positive symptoms); CHR Positive (CHR+; N=101) if they had a score of moderate to severe on any positive symptom, or as schizophrenia-like psychosis (SLP; N=35) if they had one positive symptom at a psychotic level of intensity. CHR+ and SLP patients could have attenuated negative symptoms, although this was not a requirement. For the purposes of the current study, only the CHR+ group was used because this group is most closely related to the Attenuated Positive Syndrome (APS) group which is typically studied in the prodromal literature (see Miller et al. 33). Furthermore, only CHR+ subjects with complete baseline data on self- and clinician-rated functional impairment were included. Therefore, the sample included 73 individuals at CHR for psychosis between the ages of 12 and 20. CHR+ subjects (N=28) that were not included in this study were comparable to those included, except they were rated as having more social (p=0.01) and role (p=0.02) functioning deficits, and less anxiety (p=0.04).

Patients were excluded from the study if they met DSM-IV (34) criteria for an Axis I schizophrenia-spectrum disorder (i.e., schizophrenia, schizoaffective disorder, schizophreniform disorder, or delusional disorder), major depressive disorder with psychotic features or a bipolar spectrum disorder (i.e., bipolar I, bipolar II or bipolar NOS) at baseline. Additionally, patients were excluded if they were non-English speaking, had a medical or neurological disorder that could affect brain functioning, drug or alcohol dependence within the past 6 months, or an estimated IQ below 70. Healthy control subjects (HC; N = 59) had to meet the same criteria, with the exception that they could not meet criteria for any high-risk category nor could they have a first-degree relative with a psychotic disorder. Additionally, only HC subjects with complete baseline data on self- and clinician-rated functional impairment were included. Therefore, the sample included 50 HC subjects between the ages of 12 and 22.

Clinical Assessment

All interviews for the RAP study were administered by a trained masters- or doctoral-level psychologist at the baseline visit. Axis I diagnoses were assessed by the Schedule for Affective Disorders and Schizophrenia for School-Age Children, Epidemiologic Version (KSADS-E; 35). Prodromal symptoms were assessed by the Structured Interview for Prodromal Syndromes (SIPS) and the companion Scale of Prodromal Symptoms (SOPS; 33) For the purposes of this paper, only the total scores for the positive and negative symptom subscales are analyzed. Furthermore, given that two of the negative symptom items, social anhedonia and decline in school functioning, overlap with other social and role functioning measures, these items are left out of the total negative symptom score analyses. General functioning was assessed with the Global Assessment of Functioning (GAF; 36) scale. Social and role functioning was assessed by the Global Functioning: Social scale (GF: Social; 18) and the Global Functioning: Role scale (GF: Role; 18). These rater-administered

companion scales were designed for specifically for prodromal adolescents and are rated on 1 – 10 scale with higher scores representing better functioning. The Sheehan Disability Scale (SDS; 30), a self-rated instrument, was used to measure disruption in daily functioning in social activities (i.e., relationships and leisure activities) and academic/occupational performance due to symptoms. This self-report measure asks about the impact of clinical symptoms on the subjects' social (or role) functioning on a visual-analog scale from 0 (not at all) to 10 (very severely). Depressive symptoms were assessed with the Children's Depression Inventory (CDI; 37) for children up until age 16, and the Beck Depression Inventory (BDI; 38) for youths age 17 and above. A percentage score was derived for each subject in order to combine data from the BDI and the CDI. Anxiety symptoms were assessed with the Beck Anxiety Inventory (BAI; 39).

Statistical Analyses

Data were statistically evaluated using SPSS (Chicago, Illinois, USA, Version 16.0). Missing values were imputed using the group mean. Comparisons of demographic and clinical variables were performed with an independent sample's *t*-test and chi-square analyses with group (CHR+ vs. HC) as the between-subjects factor. Correlations between clinical and functional measures were performed using the Spearman's Rho test.

Multiple regression models were used to predict baseline Sheehan Disability Scale (SDS) Social and SDS Work/School in the CHR+ group. A backward selection approach was used (probability for entry, $p \leq 0.05$; probability for removal, $p \geq 0.10$). SOPS Positive and Negative total scores, GAF, GF: Social, GF: Role, BDI/CDI percentage score, and BAI total score were entered into the models as predictor variables.

Multiple regression models were used to predict baseline GF: Social and GF: Role scores in the CHR+ group. A backward selection approach was used (probability for entry, $p \leq 0.05$; probability for removal, $p \geq 0.10$). SOPS Positive and Negative total scores, GAF, SDS Social, SDS Work/School, BDI/CDI percentage score, and BAI total score were entered into the models as predictor variables.

Results

Demographics and clinical measures

All demographic and clinical data for the CHR+ and the HC groups are presented in Table 1. The gender distribution of the two groups were comparable ($\chi^2(1) = 3.26$, $p = 0.07$), and the two groups were of comparable age ($t(121)=0.53$, $p=0.60$). But, the ethnic distribution of the CHR+ group was significantly different compared to the HC group ($\chi^2(3) = 7.95$, $p = 0.047$). The CHR+ group reported significantly higher scores on the SIPS positive total score ($t(121) = -18.74$, $p < 0.001$), SIPS negative total score ($t(121) = -16.72$, $p < 0.001$), BDI/CDI percentage score ($t(121) = -8.00$, $p < 0.001$), and the BAI total score ($t(121) = -5.18$, $p < 0.001$) compared to the HC group. The CHR+ group also reported impairment on baseline GAF ($t(121) = 26.93$, $p < 0.001$), GF: Social ($t(121) = 10.93$, $p < 0.001$), GF: Role ($t(121) = 10.12$, $p < 0.001$), SDS Social ($t(121) = -7.12$, $p < 0.001$), and SDS Work/School ($t(121) = -8.85$, $p < 0.001$) compared to the HC group.

Correlations between functional impairment and clinical measures

Table 2 presents correlations between clinical measures and SDS Social and Work/School scales. There were significant correlations between the SDS Social and all clinical measures, except the SOPS Total Positive and Negative Symptoms. Poor self-reported social functioning was related to poor clinician-rated social and role functioning, poor global functioning, and more severe depression and anxiety symptoms. There were also significant correlations between the SDS Work/School and the GF: Role, GAF, BDI/CDI and BAI. Poor self-reported work/school functioning was related to poor clinician rated role (but not social) functioning, poor global functioning, and more severe depression and anxiety symptoms.

Relating functional impairment to clinical and functioning measures

Table 3 presents the results from the linear regression model predicting baseline SDS Social scores. Baseline GF: Social and BDI/CDI scores were significant predictors of baseline SDS Social scores, with the model accounting for 32% of the variance. Although BAI scores were part of the final model, the contribution was non-significant. Table 4 presents the results from the linear regression model predicting baseline SDS Work/School scores. Baseline GF: Role, BDI/CDI scores and SOPS: Negative scores were significant predictors of baseline SDS Work/School scores, with the model accounting for 43% of the variance. Although BAI scores were part of the final model, the contribution was non-significant.

Discussion

The current study supports previous findings that individuals at CHR for psychosis are functionally impaired and extends these findings to report that these individuals recognize that their symptoms are causing a great deal of disturbance in their everyday life. Symptom-related impairment in social and role functioning, based on self-report, was significantly higher in CHR subjects than healthy control subjects. Scores on the SDS were, on average, 4 for social and 5 for work/school domains, which are scores associated with poor functioning (40) and are comparable to scores reported in individuals with schizophrenia (31, 41) and other major psychiatric disorders (42, 43). This underscores the debilitating nature of symptoms experienced by these individuals and justifies the use of early intervention strategies.

In this study, there was a strong relationship between clinician-based assessments of functioning and subjective reports of functioning. This suggests that individuals at CHR for psychosis are able to critically assess their level of functioning and recognize that their symptoms are impeding their ability to perform optimally in social and academic/occupational settings. This has also been shown in individuals with first-episode psychosis, confirming that early in the disorder patients maintain insight into their functional disabilities (15). Contrary to the findings of early stage patients, studies of patients with chronic schizophrenia report a disconnect between clinician-ratings and subjective reports of functioning (26, 27, 32), however this does not appear to be the case in CHR individuals. Thus, insight into social and role functioning remains well intact during the early phase of psychosis. It is unclear when or why insight may diminish, however this should certainly be

investigated in future studies. Overall, the data reported here suggest that individuals at CHR for psychosis are distressed by their functional impairments and the negative consequences of not being able to maintain successful relationships and achieve good academic/ occupational performance. These results suggest that self-report measures are an important addition to the assessment of pre-illness functioning.

Depressive symptoms were also significantly related to functional impairment. Our results are consistent with a number of recent studies that reported a strong relationship between depressive symptoms and functioning (16, 31, 32). In addition, symptoms of depression consistently relate to quality of life (QOL) in schizophrenia patients using both self-report and clinician-rated measures (44) Our results are not surprising, as depression is associated with a heavy disease burden (2) and schizophrenia patients with depressive symptoms have an especially poor clinical outcome (45). In CHR samples, depressive (46) or positive and negative symptoms (47) have been found to relate to QOL. However, this is the first study to report that depressive symptoms relate to the subjective assessment of functioning in a CHR population. It is possible that depression may not only have an impact on the impairment of functioning, but it may also lead to an overestimation of real impairment. Overall, the model indicates that depressive symptoms are perceived as more debilitating than prodromal symptoms.

Attenuated positive and negative symptoms were not related to subjective assessment of functioning in the current study. This is consistent with previous findings from our group (18), confirming that functioning is independent of clinical symptoms associated with the prodrome. Although it seems counterintuitive that attenuated negative symptoms did not relate to self-reported functional impairment, the attenuated negative symptom score was calculated without the social anhedonia (N1) and role deterioration (N6) items in order to prevent overlap with the respective SDS measures. In contrast, a lack of relationship between attenuated positive symptoms and functional impairment is consistent with prior work in adults with schizophrenia (48, 49). In fact, even with optimal medication treatment and remission of positive symptoms, the course of functioning is stable (21, 48, 49). Our findings have extended this notion to the early stages of the illness and confirm that the functional impairment associated with individuals at CHR is largely independent of attenuated positive symptoms (22, 50).

By elucidating what factors contribute to self-awareness of functional impairments, potential intervention strategies can be identified to target these issues and reduce the disease burden. For example, patients may be more willing to accept social skills training and supported employment (51, 52), which may help prevent long term social and role functioning impairment. Additionally, rather than directly treating attenuated positive symptoms, treating depression symptoms with antidepressants (53) or cognitive behavioral therapy (54, 55) may reduce depressive symptoms and in turn reduce perceived functional impairment. Alternative treatments, such as omega-3 fatty acids, may also be beneficial (56). There is some evidence to support that a decrease in depressive symptoms over time would result in an increase in quality of life (57). Future studies should systematically assess the effects of these treatments on symptoms and perceived functional impairment.

Limitations

The current study has some limitations that warrant consideration. First, measurements of functioning and clinical symptoms were done at baseline, therefore it is impossible to determine a causal relationship between the measures. For example, we cannot determine if depression caused a decrease in functioning, or if a decrease in functioning caused depression. Prospective studies will need to be done in order to determine if such relationships exist. Second, we had to combine two self-report measures of depression based on the age of the participant (the BDI for adults, CDI for children). The resulting score was a percentage score, rather than a total severity score. Using a single depression severity measure for all participants would have been optimal. Third, CHR+ subjects that were not included in this study were rated as having more social and role functioning deficits, and less anxiety than CHR+ subjects who were included in this study. Therefore, it is possible that our results were biased by not including more significantly impaired subjects. The CHR + subjects who were not included in the study did not complete the SDS. The SDS was added to the RAP program battery of assessments at a later time, therefore participants enrolled at the start of the program did not receive the measure.

Conclusions

This study emphasizes the importance of studying self-reports of functioning in individuals at CHR for psychosis. Although only a fraction of these individuals will go on to develop a psychotic disorder (35%; 19), the whole CHR sample, on average, reported significant functional impairment. A shift in focus from future risk for psychosis to current functional impairment is warranted in this population and may ultimately lead to a reduction in future functional impairment and conversion. In particular, based on the current findings, depressive symptoms are an important target for reducing functional impairment. Safe and effective medications and therapy should be used as a first line treatment in order to prevent long term functional impairment in at-risk samples.

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Table 1

Demographics, clinical and functioning measures.

	Healthy Controls (N=50) Mean (SD)	CHR+ (N=73) Mean (SD)
Age	16.15 (2.66)	15.92 (2.14)
Gender, N (%) male	24 (48.0%)	47 (64.4%)
Ethnicity, N (%)*		
Caucasian	30 (60.0%)	59 (80.8%)
Black	6 (12.0%)	7 (9.6%)
Asian	11 (22.0%)	5 (6.8%)
Other/Mixed	3 (6.0%)	2 (2.7%)
SOPS Total Positive, total score**	0.51 (0.83)	8.34 (3.43)
SOPS Total Negative, total score**	1.22 (1.35)	12.29 (5.42)
BDI/CDI, % score**	11.00 (9.95)	30.67 (17.27)
BAI, total score**	6.09 (6.98)	14.51 (11.03)
GAF, score**	84.50 (7.15)	46.99 (7.88)
GF: Social, score**	8.56 (0.86)	6.25 (1.48)
GF: Role, score**	8.62 (1.12)	5.85 (1.91)
SDS: Social, score**	0.88 (1.42)	4.10 (3.46)
SDS: Work/School, score**	1.08 (1.65)	5.07 (3.29)

Abbreviations: CHR+: clinical high-risk; SOPS: Scale of Prodromal Syndromes; GAF: Global Assessment of Functioning; GF: Global Functioning; SDS: Sheehan Disability Scale; BDI: Beck Depression Inventory; CDI: Children's Depression Inventory; BAI: Beck Anxiety Inventory.

* $p < 0.05$;

** $p < 0.001$

Table 2

Correlations between clinical measures and functional impairment scores in CHR+ subjects.

	SDS Social (N=73)	SDS Work/School (N=73)
SOPS Total Positive	$r = 0.16$ $p = 0.18$	$r = 0.19$, $p = 0.11$
SOPS Total Negative	$r = 0.21$, $p = 0.08$	$r = 0.07$, $p = 0.57$
GF: Social	**$r = -0.35$, $p = 0.003$**	$r = -0.07$, $p = 0.55$
GF: Role	**$r = -0.27$, $p = 0.02$**	**$r = -0.48$, $p < 0.001$**
GAF	**$r = -0.28$, $p = 0.02$**	**$r = -0.27$, $p = 0.02$**
BDI/CDI	**$r = 0.41$, $p < 0.001$**	**$r = 0.50$, $p < 0.001$**
BAI	**$r = 0.40$, $p < 0.001$**	**$r = 0.47$, $p < 0.001$**

Significant correlations are in bold.

Abbreviations: CHR+: clinical high-risk; SOPS: Scale of Prodromal Syndromes; GAF: Global Assessment of Functioning; GF: Global Functioning; SDS: Sheehan Disability Scale; BDI: Beck Depression Inventory; CDI: Children's Depression Inventory; BAI: Beck Anxiety Inventory.

Table 3

Significant predictors of SDS Social in CHR+ subjects (N=73).

Predictor Variable	Regression coefficient (b)	Standard error (SE)	β	Confidence Intervals	*p*-value
CHR+ (N=73)					
GF: Social	−0.82	0.23	−0.35	−1.27 - −0.36	< 0.001
BDI/CDI	0.06	0.03	0.29	0.01 - 0.11	0.02
BAI	0.08	0.04	0.24	0.00 - 0.15	0.05

CHR+, adjusted $R^2 = 0.32$.

Abbreviations: b, unstandardized beta coefficient; β, standardized beta coefficient; R^2, how much variation is being explained by the predictor variables. CHR+: clinical high-risk; GF: Global Functioning; BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; CDI: Children's Depression Inventory; SDS: Sheehan Disability Scale.

Table 4

Significant predictors of SDS Work/School in CHR+ subjects (N = 73).

Predictor Variable	Regression coefficient (b)	Standard error (SE)	β	Confidence Intervals	*p*-value
GF: Role	−0.79	0.17	−0.46	−1.12 - −0.45	< 0.001
BDI/CDI	0.06	0.02	0.31	0.02 - 0.10	0.01
SOPS: Negative	−0.18	0.09	−0.20	−0.36 - −0.01	0.04
BAI	0.07	0.03	0.22	−0.00 – 0.14	0.06

Adjusted $R^2 = 0.43$.

Abbreviations: b, unstandardized beta coefficient; β, standardized beta coefficient; R^2, how much variation is being explained by the predictor variables. CHR+: clinical high-risk; GF: Global Functioning; BAI; Beck Anxiety Inventory; BDI: Beck Depression Inventory; CDI: Children's Depression Inventory; SDS: Sheehan Disability Scale; SOPS: Scale of Prodromal Symptoms.