Schizophrenia Bulletin vol. 40 no. 6 pp. 1452–1461, 2014
doi:10.1093/schbul/sbt235
Advance Access publication February 18, 2014

The Relationship of Neurocognition and Negative Symptoms to Social and Role Functioning Over Time in Individuals at Clinical High Risk in the First Phase of the North American Prodrome Longitudinal Study

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Objectives: **Impaired social, role, and neurocognitive functioning are preillness characteristics of people who later develop psychosis. In people with schizophrenia, neurocognition and negative symptoms are associated with functional impairment. We examined the relative contributions of neurocognition and symptoms to social and role functioning over time in clinically high-risk (CHR) individuals and determined if negative symptoms mediated the influence of cognition on functioning.** ***Methods:*** **Social, role, and neurocognitive functioning and positive, negative, and disorganized symptoms were assessed in 167 individuals at CHR for psychosis in the North American Prodrome Longitudinal Study Phase 1 (NAPLS-1), of whom 96 were reassessed at 12 months.** ***Results:*** **Regression analyses indicated that negative symptoms accounted for unique variance in social and role functioning at baseline and follow-up. Composite neurocognition accounted for unique, but modest, variance in social and role functioning at baseline and in role functioning at follow-up. Negative symptoms mediated the relationship between composite neurocognition and social and role functioning across time points. In exploratory analyses, individual tests (IQ estimate, Digit Symbol/Coding, verbal memory) selectively accounted for social and role functioning at baseline and follow-up after accounting for symptoms. When negative symptom items with content overlapping with social and role functioning measures were removed, the relationship between neurocognition and social and role functioning was strengthened.** ***Conclusion:*** **The modest overlap among neurocognition, negative symptoms, and social and role functioning indicates that these domains make substantially separate contributions to CHR individuals.**

Key words: social and role functioning/neurocognition/negative symptoms/prodrome

The search for robust clinical indicators of psychosis and associated disability has accelerated with the gradual acceptance of the clinical high-risk (CHR) phase prior to psychosis ("putative prodrome").[1–3] In the neurodevelopmental model proposed by Cornblatt and colleagues,[4] psychosis vulnerability involves deficits in at least 4 clinically measureable domains (*C*ognitive-*A*ffective-*S*ocial *I*solation-*S*chool/work problems) referred to as the "CASIS" cluster that are thought to develop relatively independently of positive symptoms. There is substantial support for this model in that neurocognitive and functional (eg, impaired social and role functioning) deficits are present prior to and during the CHR phase.[4–9] Greater neurocognitive impairments prospectively predict conversion to psychosis among CHR participants.[6,10,11] Negative symptoms predict transition to psychosis among people at CHR.[1,12] Social difficulties also predict conversion among people at CHR after accounting for attenuated positive symptoms.[1–3] Impairment in social

and role functioning is a central aspect of the persistent difficulties experienced by many people at CHR, regardless of whether they transition to psychosis.[5,13–15] Our goal is to focus on an understudied area in CHR research: the relative contributions of neurocognition and symptoms to functional outcomes over time in CHR participants, including whether negative symptoms mediate the impact of neurocognition on social and role functioning in CHR, based on the schizophrenia literature.[16]

The notion that domains of neurocognitive impairment are related to social or role impairment in schizophrenia was first demonstrated by Green and colleagues, initially in chronic schizophrenia samples.[17] More recent research supports the relationship between neurocognition and functional outcomes in recent-onset psychosis.[18–21] A meta-analysis found that negative symptoms were associated with functional outcomes in schizophrenia, in contrast to the negligible relationship between positive symptoms and functional outcomes.[16] Negative symptoms also prospectively predicted functioning in first-episode schizophrenia.[22] While prior findings suggest that neurocognition may be a stronger predictor of functioning than symptoms in schizophrenia,[23,24] some have questioned the extent to which neurocognition predicts functioning independent of symptoms.[25,26] In chronic and first-episode schizophrenia, negative symptoms are moderately associated with neurocognition,[16,27–32] with smaller associations between disorganized symptoms and cognition,[31–34] and weak relationships between positive symptoms and neurocognition.[16,29] Thus, the joint impact of negative symptoms and neurocognition on function requires more study, particularly in longitudinal CHR studies.[16]

Several studies examined some relations among these constructs in CHR samples. In a small study of 22 participants, baseline disorganized symptoms and executive functioning deficits predicted self-reported social functioning at 1-year follow-up, and baseline deficits in executive functioning and processing speed predicted self-reported work functioning at follow-up.[35] By contrast, in a study of 35 participants, neither baseline neurocognitive functioning nor clinical symptoms predicted social or role functioning at 8 months.[36] In a large study of 230 participants with an average follow-up duration of 7 years, baseline negative symptoms and poor verbal memory predicted poor functional outcomes at follow-up.[13] Tests of processing speed and verbal fluency also emerged as prospective predictors of poor functioning in subsamples of participants. In another study, social and role functioning deficits were associated with worse processing speed and global neurocognition at baseline.[37] These findings were independent of positive symptoms, although negative and disorganized symptoms were not examined. At 3-year follow-up with this sample, disorganized symptoms and worse processing speed predicted impaired social functioning, while disorganized symptoms and motor disturbances predicted impaired role functioning.[38]

In the current study, we examined the contributions of symptoms and a composite neurocognition score to social and role functioning at baseline and 12-month follow-up among CHR individuals from the North American Prodrome Longitudinal Study Phase 1 (NAPLS-1). We hypothesized that (1) negative symptoms would be more strongly associated with social and role functioning than positive or disorganized symptoms, (2) negative symptoms and neurocognition would each account for unique variance in social and role functioning at baseline, (3) baseline composite neurocognition and negative symptoms would each independently predict social and role functioning at 12-month follow-up, and (4) negative symptoms would mediate the relationship between neurocognition and social and role functioning at baseline and at 12 months. Based on prior research,[13,18,32,36,37] we explored whether certain individual neurocognitive tests (IQ, processing speed, verbal memory) accounted for social and role functioning cross-sectionally and at 12 months after controlling for baseline symptoms.

Methods

Study protocols and informed consent documents, including procedures, were approved by the Institutional Review Boards of the 8 participating sites. NAPLS-1 methods and details of the federated database are described elsewhere.[3,6]

Sample

The NAPLS-1 CHR sample consisted of 370 individuals who met the Criteria of Prodromal Syndromes (COPS), based on the Structured Interview for Prodromal Syndromes (SIPS),[39] of whom 35% converted to psychosis over 30 months.[3] The participants ranged from 12 to 36 years of age and had IQs of at least 70. The current sample is the identical subsample (n = 167) who completed a minimum of 75% of the most commonly administered neurocognitive tests in the NAPLS-1 federated baseline database (ie, 6 or more of 8 tests) and for whom a composite cognition score was computed.[6] That report,[6] which details the neurocognitive methodology, indicated that this subsample did not differ on any demographic characteristic from the larger NAPLS-1 CHR sample. We conducted additional T tests indicating that this subsample was not significantly different from the remaining NAPLS-1 sample in baseline social or role functioning or in positive, negative, or disorganized symptoms (P values > .21). About one-third of this subsample was included in a prior NAPLS-1 study examining predictors of social and role functioning,[5] although that article did not focus on neurocognition or address the relationship between neurocognition and negative symptoms in predicting functioning, and 23% overlap with another recently published study.[38] Of the 167 participants included here, 96

and 94 completed the measure of social and role functioning at 12-month follow-up, respectively.

Measures

CHR Status and Clinical Symptoms. The SIPS criteria[39] was used for study entry. About 97% of CHR individuals met full criteria for Attenuated Positive Symptom (APS) Syndrome, which emphasizes onset or worsening of attenuated positive symptoms in the past 12 months, in at least one of the 5 positive symptom domains: unusual thought content, suspiciousness/paranoia, grandiosity, perceptual anomalies, and conceptual disorganization. In addition to attenuated positive symptoms (SIPS-Positive), we assessed SIPS-Negative (social anhedonia or withdrawal, avolition, decreased expression of emotions, decreased experience of emotions and self, decreased ideational richness, deterioration in role functioning) and SIPS-Disorganized (odd behavior or appearance, bizarre thinking, trouble with focus and attention, personal hygiene/social attentiveness). Symptom domain scores are the sum of symptom severity scores.

Social and Role Functioning. Social and role functioning was assessed using the GF: Social and GF: Role scales.[40] These rater-scored measures were designed as parallel, well-anchored scales that account for age and phase of illness and detect functional changes over time.[40] GF: Social assesses peer relationships, peer conflict, age appropriate intimate relationships, and involvement with family members. GF: Role assesses performance and amount of support needed in one's specific roles (ie, school/work). Scores range from 1 to 10 (10 = superior functioning to 1 = extreme dysfunction). Scores around 6 typically characterize CHR individuals.[40] Current (ie, past month) scores were used in the current study. In NAPLS-1, ratings for each scale were based on best estimates derived from all available information.[40] This approach has been used in prior reports[3,5,15] and exhibited high interrater reliability.[2]

Neurocognitive Assessment. The tests and domains included were as follows: verbal comprehension (Vocabulary), visual-perceptual-organization (Block Design), vigilance (Continuous Performance Test-Identical Pairs Version), processing speed (Digit Symbol/Coding), executive functioning including verbal fluency (Controlled Oral Word Association test [COWA]) and problem solving (Wisconsin Card Sorting Test [WCST] perseverative errors), and a verbal memory composite score. These tests are representative of those sensitive to impairments in CHR individuals.[10,11] A small proportion (7.3%) of the test scores were missing. A composite neurocognition score was constructed as the standardized mean of the test scores. For the exploratory analyses examining individual test scores, we examined Full Scale IQ (FSIQ) estimates. Additional detail regarding the tests, missing data, and computation of the composite score can be found in table 3, in an online supplementary data, and in a prior report.[6]

Statistical Analyses

Statistical analyses were performed using IBM SPSS version 20. Preliminary between-groups analyses were conducted to examine the comparability of participants who completed GF: Social and GF: Role at 12-month follow-up with those who did not. Correlational analyses were conducted to examine the relations among cognitive tests, SIPS symptoms, GF: Social, and GF: Role. Simultaneous regression analyses were conducted to test the hypotheses that (1) SIPS-Negative symptoms would be more strongly associated with GF: Social and GF: Role than SIPS-Positive or SIPS-Disorganized, (2) SIPS-Negative and composite cognition would independently account for unique variance in GF: Social and GF: Role cross-sectionally, and (3) baseline SIPS-Negative and composite cognition would independently predict GF: Social and GF: Role at 12-month follow-up. We examined the influence of content overlap between SIPS-Negative and the functioning measures by rerunning the primary regression models after removing overlapping items. Specifically, we reran the models predicting GF: Social after removing the SIPS-Negative item tapping social anhedonia or withdrawal and the models predicting GF: Role after removing the item tapping deterioration in role functioning. Next, we tested the hypothesis that SIPS-Negative would mediate the relations between cognition and GF: Social and GF: Role at baseline and follow-up using Sobel tests. Finally, we explored whether selected cognitive tests (FSIQ estimate, Digit Symbol/Coding, verbal memory) accounted for GF: Social and GF: Role at baseline and follow-up, controlling for symptoms, using simultaneous regressions.

Results

Primary Analyses

Participant characteristics are listed in table 1. Participants who completed GF: Social and GF: Role at 12-month follow-up did not differ from those who did not on baseline functioning (table 2). A paired-sample *t*-test indicated that GF: Social improved at 12 months in the follow-up sample, $t(95) = 3.15$, $P = .002$ as did GF: Role, $t(93) = 4.60$, $P < .001$. *T* tests indicated that the follow-up sample did not differ from the rest of the sample on baseline composite neurocognition or any SIPS symptom domain (*P* values = .11–.52).

Pearson product-moment correlations among the neurocognitive tests, SIPS symptom domains, GF: Social, and GF: Role are presented in table 3. Among the symptom domains, SIPS-Negative was most strongly associated with neurocognition, though the correlations were

modest, followed by SIPS-Disorganized. SIPS-Positive was only marginally associated with one cognitive test and was not associated with the composite score. All neurocognitive tests were modestly associated with GF: Social at baseline. Most neurocognitive tests were modestly associated with GF: Social at follow-up, with the exception of Block Design and COWA. Similarly, most neurocognitive tests were modestly associated with GF: Role at baseline and follow-up, with the exception of Block Design at both time points and COWA at follow-up. SIPS-Negative was most strongly associated with GF: Social and GF: Role at baseline and follow-up, followed by SIPS-Disorganized. SIPS-Positive was not associated with GF: Social or GF: Role at either time point. GF: Social was moderately associated with GF: Role at baseline, and this association became stronger at follow-up. The test-retest reliability coefficients were .69 for GF: Social and .50 for GF: Role.

All variables included in regression analyses were normally distributed. Simultaneous regression analyses were conducted in which baseline SIPS symptom clusters and composite cognition score were entered as predictors, and GF: Social and GF: Role at baseline and follow-up were the outcomes (table 4). At baseline, both models were significant, accounting for 36% of the variance in GF: Social and 35% of the variance in GF: Role. SIPS-Negative was most strongly associated with functioning at both time points. SIPS-Negative ($\beta = -.390$; $P < .001$) and composite neurocognition ($\beta = .175$; $P = .013$) each accounted for unique variance in GF: Social at baseline. Similarly, both SIPS-Negative ($\beta = -.413$; $P < .001$) and composite neurocognition ($\beta = .153$; $P = .036$) were associated with GF: Role at baseline. At follow-up, both models were again significant, accounting for 32% of the variance in GF: Social and 25% of the variance in GF: Role. SIPS-Negative ($\beta = -.447$; $P < .001$) was the only significant predictor of GF: Social at follow-up. Both SIPS-Negative ($\beta = -.398$; $P = .002$) and composite neurocognition ($\beta = .232$; $P = .028$) were significant predictors of GF: Role at follow-up. Neither SIPS-Disorganized nor SIPS-Positive were associated with social or role functioning at either time point.

Table 1. Participant Characteristics

	M	SD
Age (y)	18.2	4.9
Education (y)	10.4	3.1
Parental education[a]	5.4	1.6
	n	%
Male gender	107	64.1
Taking antipsychotic medication	6	3.6
White race	139	83.2
African American race	15	9.0
Asian American	6	3.6
Multiracial	7	4.2
Hispanic ethnicity	23	13.8

Note: [a]Parental education was assessed on the following scale: 1 (less than high school); 2 (some high school); 3 (high school graduate); 4 (some college); 5 (associate's degree); 6 (bachelor's degree); 7 (some postgraduate education); and 8 (graduate degree).

Modified Analyses After Removing Select Negative Symptom Items

We examined the influence of content overlap in assessing the relationship between negative symptoms and functioning (table 5). The models predicting GF: Social and GF: Role at baseline and follow-up remained significant (all *P* values remained <.001), though the amount of variance in functioning explained by these models (ie, total R^2) decreased by 17% on average. The magnitude of the associations between SIPS-Negative and functioning (ie, standardized regression coefficients) decreased in each case by an average of 40%. Conversely, the magnitude of the relations between composite neurocognition and functioning and SIPS-Disorganized and functioning increased by an average of 21% and 34%, respectively. When the overlapping symptoms were removed from SIPS-Negative, the magnitude of the associations between composite

Table 2. Social and Role Functioning Scores by Follow-up Status

	Participants Who Completed Measures at Follow-up		Participants Who Did Not Complete Follow-up Measures		Test Statistic (*t*)
	M	SD	*M*	SD	
GF: Social (baseline)	6.40	1.7	5.95	1.4	1.81
GF: Social (follow-up)	6.82	1.6	—	—	—
GF: Role (baseline)	6.26	1.8	6.11	1.5	0.56
GF: Role (follow-up)	7.04	1.5	—	—	—

Note: GF: Social, Global Social Functioning Scale; GF: Role, Global Role Functioning Scale. Follow-up *n* for GF: Social = 96. Follow-up *n* for GF: Role = 94.
*$P < .05$, **$P < .01$, ***$P < .001$ (none were significant).

Table 3. Correlations Between Neuropsychological Test Performance and Psychiatric Symptoms and Social and Role Functioning at Baseline and 12-Month Follow-up

	SIPS-Positive Symptoms Total	SIPS-Disorganized Symptoms Total	SIPS-Negative Symptoms Total	SIPS Social Anhedonia or Withdrawal	SIPS Avolition	SIPS Decreased Expression of Emotions	SIPS Decreased Experience of Emotions and Self	SIPS Decreased Ideational Richness	SIPS Deterioration in Role Functioning	GF: Social (BL)	GF: Social (FU)	GF: Role (BL)	GF: Role (FU)
Vocabulary ScS	−.07	−.18*	−.21**	−.10	−.003	−.10	−.07	−.41***	−.24**	.27***	.21*	.26**	.37*
Block Design ScS	.09	−.07	−.15	−.08	−.05	−.09	−.05	−.22**	−.12	.18*	.07	.11	.05
Digit Symbol/ Coding ScS	.17*	−.15	−.34***	−.28***	−.18*	−.24**	−.03	−.21**	−.38***	.34***	.36***	.31***	.26*
TMT-B (s)	.09	−.07	−.21**	−.06	−.19*	−.13	.05	−.27**	−.27**	.20*	.22*	.27**	.22*
CPT-IP Digits d’	.11	−.21*	−.32***	−.16	−.23**	−.14	−.10	−.23*	−.35***	.25**	.26*	.24**	.38**
COWA Raw Score	.04	−.22**	−.24**	−.08	−.14	−.19*	.02	−.24**	−.32***	.25**	.11	.21**	.12
WCST persev. errors	.08	−.19*	−.33***	−.19*	−.20*	−.23**	−.07	−.33***	−.32***	.24**	.33**	.28***	.27**
Verbal Memory	.01	−.14	−.30***	−.15	−.10	−.10	−.10	−.45***	−.25**	.29***	.25*	.19*	.32**
Composite score	.09	−.21**	−.37***	−.19*	−.20*	−.22**	−.06	−.43***	−.39***	.35***	.32**	.33***	.36***
GF: Social (BL)	−.15	−.46***	−.56***	−.63***	−.25**	−.42***	−.09	−.39***	−.40***	—	.69***	.41***	.54***
GF: Social (FU)	.09	−.42***	−.56***	−.69***	−.35***	−.33**	−.06	−.29**	−.49***	.69***	—	.40***	.66***
GF: Role (BL)	−.08	−.40***	−.54***	−.34***	−.37***	−.35***	−.16*	−.18*	−.70***	.41***	.40***	—	.50***
GF: Role (FU)	−.04	−.28**	−.46***	−.43***	−.30**	−.19	−.14	−.25*	−.45***	.54***	.66***	.50***	—

Note: BL, baseline; FU, follow-up; SIPS symptom totals, Structured Interview for Prodromal Symptoms total symptom severity; GF: Social, Global Social Functioning Scale; GF: Role, Global Role Functioning Scale; Wechsler subtests (Vocabulary, Block Design, Digit Symbol/Coding) are (age corrected) scaled scores (ScS); TMT-B, Trail Making Test “B” in seconds (reverse scored so that higher scores indicate better performance); CPT-IP Digits d’ is the Continuous Performance Test-Identical Pairs (digits) signal detection measure of discriminability; COWA (Controlled Oral Word Association test) is a raw score (total words generated); WCST persev. errors is a raw score on the Wisconsin Card Sorting Test perseverative errors (reverse scored so that higher scores indicate better performance); Verbal Memory is a composite of (1) List Learning: Percentage correct across trials on Hopkins Verbal Learning Test, Rey Auditory Verbal Learning Test, or California Verbal Learning Test (adult and child versions) and standardized against a normal control group and (2) Story Recall: percentage of units recalled on immediate recall condition for Children’s Memory Stories, Wechsler Memory Scale–Revised, and Wechsler Memory Scale-Third revision - Logical Memory I and standardized against a normal control group; composite score is the mean standardized score of the 8 measures standardized against a normal control group; proportion of missing data by test is: WCST perseverative errors (30.8% missing), CPT-IP Digits d’ (14.8%), Verbal Memory (4.0%), Coding (2.8%), TMT-B (2.5%), Vocabulary (2.2%), Block Design (1.5%), and COWA (0%).
*$P < .05$, **$P < .01$, ***$P < .001$.

Table 4. Regression Analyses Examining Predictors of Social and Role Functioning at Baseline and 12-Month Follow-up

	GF: Social (Baseline)	GF: Social (Follow-up)	GF: Role (Baseline)	GF: Role (Follow-up)
Baseline Predictor	β	β	β	β
SIPS-Positive	−.037	.136	.024	−.067
SIPS-Negative	−.390***	−.447***	−.413***	−.398**
SIPS-Disorganized	−.166	−.134	−.117	.055
Composite cognition	.175*	.085	.153*	.232*
Total R^2	.363***	.345***	.318***	.253***

Note: β, standardized regression coefficients. Abbreviations are explained in the first footnote to tables 2 and 3.
*P < .05, **P < .01, ***P < .001.

Table 5. Regression Analyses Examining Predictors of Social and Role Functioning at Baseline and 12-Month Follow-up After Removing Negative Symptoms That Overlap With Functioning

	GF: Social (Baseline)	GF: Social (Follow-up)	GF: Role (Baseline)	GF: Role (Follow-up)
Baseline Predictor	β	β	β	β
SIPS-Positive	−.027	.150	.043	−.056
SIPS-Negative	−.207*	−.246*	−.221*	−.314*
SIPS-Disorganized	−.283**	−.263*	−.238*	−.004
Composite cognition	.214**	.123	.208**	.259*
Total R^2	.305***	.272***	.254***	.227***

Note: β, standardized regression coefficients. Abbreviations are explained in the first footnote to tables 2 and 3. The SIPS-Negative item tapping social anhedonia or withdrawal was removed from analyses of GF: Social. The SIPS-Negative item tapping deterioration in role functioning was removed from analyses of GF: Role.
*P < .05, **P < .01, ***P < .001.

neurocognition and/or SIPS-Disorganized and functioning were roughly equivalent to those of SIPS-Negative.

Mediation Analyses

We used Sobel tests[41] to examine whether SIPS-Negative mediated the relations between composite neurocognition and GF: Social and GF: Role at baseline and follow-up. Evidence for mediation would be observed if: (1) composite neurocognition significantly affects SIPS-Negative, (2) neurocognition significantly affects GF: Social and GF: Role in the absence of SIPS-Negative, (3) SIPS-Negative has a significant, unique effect on functioning, and (4) the effect of neurocognition on functioning shrinks when SIPS-Negative is added to the model. A significant result with the Sobel test is evidence of partial mediation and does not make any claim regarding full mediation. In each case, the Sobel test was highly significant (test values ranged from 2.98 to 4.14; P values from .003 to <.001), indicating that SIPS-Negative mediated the relations between cognition and GF: Social and GF: Role at baseline and follow-up. Removing the respective overlapping symptoms yielded the same finding that SIPS-Negative mediated the effects of cognition on GF: Social and GF: Role at baseline and follow-up (Sobel test values = 2.59–3.72; P values = .01 to <.001).

Exploratory Analyses Using Individual Tests

We explored whether selected individual baseline neurocognitive tests accounted for GF: Social and GF: Role, controlling for symptoms, at baseline and follow-up using simultaneous regression analyses (supplementary tables S1a–S3a). SIPS symptom domains were entered into each regression model, along with FSIQ estimate, Digit Symbol/Coding, and verbal memory in separate models. All models were significant and accounted for approximately the same amount of variance in functioning as the primary regressions that included the composite neurocognition score. Both IQ estimate and Digit Symbol/Coding accounted for unique variance in GF: Social at baseline only (β = .164, P = .013 and β = .141, P = .048, respectively) and did not account for unique variance in GF: Role at either time point. Verbal memory did not account for GF: Social or GF: Role at baseline but did predict GF: Role at follow-up (β = .218, P = .040). Removing the overlapping items from SIPS-Negative increased the magnitude of the relations between these individual cognitive tests and functioning (supplementary tables S1b–S3b). Specifically, IQ estimate continued to account for unique variance in GF: Social (β = .18, P = .01) and became significant for GF: Role at baseline (β = .16, P = .026). Digit Symbol/Coding continued to account for unique

variance in GF: Social at baseline (β = .188, *P* = .011) and became a significant predictor of GF: Social at follow-up (β = .193, *P* = .049) and of GF: Role at baseline (β = .201, *P* = .008). Verbal memory became significant for GF: Social at baseline (β = .171, *P* = .024) and continued to predict GF: Role at follow-up (β = .233, *P* = .032).

Discussion

The results of the primary analyses generally supported our hypotheses and shed new light on the relationship of neurocognition and negative symptoms in CHR individuals. First, the findings are generally consistent with research on chronic and first-episode schizophrenia studies in terms of the influence of neurocognition and symptoms on functioning. In baseline correlational analyses, worse performance on neurocognitive tests and composite neurocognition was most strongly associated with negative symptom severity, followed by disorganized symptom severity, whereas positive symptoms were not meaningfully associated with neurocognition. As hypothesized, in regression analyses, we found that negative symptoms were associated with social and role functioning at both time points, whereas neither positive nor disorganized symptoms accounted for unique variance in functioning at either time point. This finding is consistent with most prior research in CHR[13] and schizophrenia[16] samples, although few prior studies examined disorganized symptoms. Next, as hypothesized, we found that composite neurocognition accounted for unique variance in social and role functioning at baseline after accounting for symptoms. We found partial support for our hypothesis regarding the prospective analyses, as baseline composite neurocognition accounted for unique variance in role, but not social functioning at 12-month follow-up after accounting for baseline symptoms. In the primary analyses, negative symptoms were the strongest predictor of social and role functioning at baseline and 12-month follow-up and had small-to-medium effects, followed by composite neurocognition, which had small independent effects. In exploratory analyses, individual tests (IQ estimate, Digit Symbol/Coding, verbal memory) selectively accounted for functioning at baseline and follow-up after accounting for symptoms, which is consistent with prior CHR studies.[13,35,38] Finally, negative symptoms did indeed mediate the relationship between neurocognition and social and role functioning at both time points.

An important methodological issue was noted in these analyses. That is, 2 items in the SIPS negative symptom scale overlap with one item each on the social and role functioning scales. Specifically, the SIPS-Negative scale contains 2 symptoms, "social anhedonia or withdrawal" and "deterioration in role functioning" that overlap with social and role functioning, respectively. When these overlapping items were removed, the magnitude of the relationship between negative symptoms and functioning was reduced substantially. Conversely, the magnitude of the relations between composite neurocognition and functioning and between disorganized symptoms and functioning both increased substantially and became roughly equivalent to the relationship between negative symptoms and functioning. These supplementary findings with respect to disorganized symptoms are consistent with 2 prior CHR studies that found that disorganized symptoms, not positive or negative symptoms, prospectively predicted functional outcomes.[35,38] This convergence in findings, in part, could be due to some small overlap (23%) between the current sample and one of the prior studies.[38] Removing the overlapping items resulted in Digit Symbol/Coding becoming a significant predictor of 12-month social functioning. Item overlap did not influence the findings regarding negative symptoms as a mediator of the relationship between composite neurocognition and functioning. Further complicating this issue with respect to the SIPS-Negative scale is that the item tapping "social anhedonia or withdrawal" may be viewed as combining a symptom (anhedonia) with an aspect of functioning (withdrawal). This issue warrants increased attention in future investigations of the relationship between negative symptoms and functional outcomes.

Negative symptoms mediated the relationship between composite neurocognition and social and role functioning both at baseline and at 12-month follow-up. This replicates the findings of a meta-analysis of schizophrenia studies[16] and extends the finding to CHR participants. Moreover, the current study was the first to examine mediation longitudinally in CHR participants, which is important for validating this relationship between neurocognition and negative symptoms as it relates to functioning. As noted previously,[16] the designation of cognition as the predictor (IV) and negative symptoms as the mediator may be viewed as somewhat arbitrary. To support this approach, we relied on theory, evidence documenting early premorbid cognitive deficits in those who eventually develop psychosis,[7,9] and lack of strong evidence suggesting that negative symptoms cause neurocognitive deficits. The finding that negative symptoms mediated the effect of neurocognition on social and role functioning across time has implications for treatment with CHR individuals. Overall, these findings support the rationale for integrative psychosocial rehabilitation programs for early psychosis that target both negative symptoms and neurocognition as a means of improving functioning.

The observation of a more modest relationship between neurocognition and functioning in CHR samples than in schizophrenia[42] is important. This may suggest, in part, that the CHR syndrome reflects a changing phase of illness in which some individuals go on to develop psychosis (and not all schizophrenia), others remain somewhat stably impaired, and a third subgroup improves.[15] This contrasts with the relative stability of samples of patients with

schizophrenia in which both neurocognition and social and role impairments are more likely to be stable. Moreover, neurocognitive impairments among CHR individuals as a whole, compared to converters, are relatively mild[6] and may have a weaker impact on functioning. The contribution of neurocognition was somewhat stronger for role, compared to social functioning, over time. In both the primary analyses and the analyses adjusting for overlapping symptoms, the magnitude of the relationship between neurocognition and role functioning increased slightly over time, whereas the relationship between neurocognition and social functioning decreased and became nonsignificant at follow-up. The aspects of neurocognitive functioning (memory, attention, processing speed, and so forth) assessed in this study may have greater independent associations with role functions such as school or job-related tasks over time than with social functioning. Social cognition, which was not assessed in this study, appears to be more strongly associated with social functioning over time.[43]

The current findings should be interpreted in the context of several limitations. First, because NAPLS-1 participants were drawn from different studies and combined in a federated database, the full complement of measures administered in these studies could not be used. This was particularly true for neurocognitive measures, as only a modest subset was given across sites.[6] In particular, the verbal memory measure was an amalgam of different measures. Nevertheless, these measures are typical of those given in other studies and represent a reasonable assessment of neurocognitive functioning in the prodrome.[10,11] Of the tests included, the rate of missing test scores was low. Second, this study used a set of common clinical neuropsychological tests, most of which tap multiple aspects of cognition, and in theory they may not be optimal for elucidating relations among symptoms, cognition, and functioning. In terms of future directions, it may be more likely that studies linking social cognition[43] and more specific aspects of cognition (ie, a cognitive neuroscience approach)[44] will elucidate relations with specific symptoms and aspects of functioning. Next, while the sample was reasonably large, only a subset completed the functioning measures at follow-up. Future research, including NAPLS-2,[45] can address these issues with a larger sample and a more sophisticated neurocognitive battery. Next, in addition to content overlap, method variance may have influenced the relations between symptoms and functioning, as the same raters used clinical judgment in assessing both constructs. Multimethod approaches to assessing functioning are recommended for use in future research, including performance-based or functional capacity measures[46] and measures of motivation.[47] Exploring mediators and mechanisms of action in integrative rehabilitation programs may also be helpful by clarifying whether, for example, such programs improve functioning by modifying aspects of neurocognition or by reducing negative symptoms. Individual participant predictor models can be tested and likely enhanced by the joint use of neurocognition, social and role functioning, and symptoms, all of which are sufficiently independent to warrant inclusion in multivariate prediction models. Finally, given that initial meta-analyses of treatment of CHR individuals are promising,[48] it is possible that a new generation of specific treatments designed to improve neurocognition and negative and disorganized symptoms will further improve the lives of CHR individuals.

Funding

National Institute of Mental Health of the National Institutes of Health (U01 MH081928 to L.J.S., U01 MH066134 to J.A., R01 MH60720 to K.S.C., R01 MH065079 to T.D.C., R01 MH061523 to B.A.C., U01 MH066069 to D.O.P., RO1MH062066 to E.F.W., U01 MH066160 to S.W.W., K05MH01654 to T.H.M.), and the Commonwealth of Massachusetts (SCDMH82101008006 to L.J.S.).

Acknowledgments

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The authors have declared that there are no conflicts of interest in relation to the subject of this study.

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