Social Cognition Deficits Among Individuals at Familial High Risk for Schizophrenia

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Social cognition in young relatives of schizophrenia probands ($N = 70$) and healthy controls ($N = 63$) was assessed using the Penn Emotion Recognition Test-40 to examine the presence of social cognitive deficits in individuals at risk for the disorder. Measures of neurocognitive function and prodromal psychopathology were collected to assess the cognitive and clinical correlates of social cognitive impairments in at-risk relatives. Results indicated that when compared with healthy controls, individuals at familial high risk for schizophrenia were significantly more likely to overattribute emotions to neutral faces, with such individuals frequently misinterpreting neutral faces as negative. In addition, at-risk individuals had significantly greater reaction times when completing emotion recognition tasks, regardless of valence. Impairments in neurocognition were largely independent of social cognitive performance, and emotion recognition impairments persisted after adjusting for deficits in neurocognitive function. Further, social cognitive impairments in the interpretation of neutral faces were significantly associated with greater positive and general prodromal psychopathology, whereas neurocognitive impairments were only associated with disorganization. These results suggest that impairments in social cognition may be unique endophenotypes for schizophrenia.

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Schizophrenia is a chronic and disabling disorder that is characterized by significant impairments in social and nonsocial cognition. Individuals with schizophrenia have for some time been shown to have marked neurocognitive deficits in attention, working memory, and executive functioning;[1] and growing evidence indicates that deficits are also prominent in such social cognitive domains as emotion perception,[2] social cue recognition,[3] interpersonal attribution,[4] and perspective taking and theory of mind.[5] Longitudinal studies have shown that many of these domains of cognitive impairment are stable over time and are present even after the remission of psychotic symptoms.[6,7] Recent investigations have not only highlighted the presence and stability of deficits in social and nonsocial cognition in schizophrenia but also underscored the centrality of these impairments in schizophrenic illness by showing consistent and robust relations between cognition and functional outcome in this population.[8,9]

The frequency, pervasiveness, and stability of cognitive impairment in schizophrenia have led investigators to posit endophenotypic models of the illness with neurobiologically based impairments in cognitive function as a core component.[10,11] Support has been garnered for such models in recent years from studies documenting the presence of similar cognitive deficits in patients with schizophrenia and their unaffected relatives,[12] although cognitive dysfunction in unaffected relatives appears to be milder than in schizophrenia.[13] Unfortunately, the majority of these investigations have focused primarily on the heritability of neurocognitive impairments in attention, working memory, and executive functioning, whereas deficits in social cognition have received little attention in the endophenotyping literature. Although impairments in social cognition have been increasingly recognized as separate, but related to neurocognitive dysfunction,[14,15] and convincing theoretical and empirical models suggest that social cognitive impairment may underlie the development of schizophrenic symptoms and disability,[16,17] little is known about the degree to which impairments in social cognitive functioning represent endophenotypic markers of the illness.

To date, only a few studies have examined the heritability of social cognitive impairment in schizophrenia through the use of samples at heightened genetic risk for the illness. One study by Kee et al[18] found that siblings

of patients with schizophrenia performed moderately worse on a series of emotion perception tasks (particularly in facial emotion perception tasks) than healthy controls but slightly better than their affected relatives. Another study of unaffected siblings of patients with schizophrenia by Leppänen et al[19] was consistent with these findings, where these investigators demonstrated significant performance impairments in the recognition of facial displays of anger in unaffected siblings relative to healthy controls, further supporting social cognitive deficits in emotion perception as a potential endophenotype for schizophrenia. Recently, Addington et al[20] extended this line of investigation to the schizophrenia prodrome, where they found that individuals at clinical high risk for developing schizophrenia performed as poorly as first-episode schizophrenia patients on an emotion identification task. Taken together, these findings increasingly suggest that impairments in perhaps the most widely studied domain of social cognition in schizophrenia, emotion perception, may be a marker of genetic liability for the disorder and eventually portend who will develop the illness.

While these studies have provided promising results pointing to social cognitive impairment in emotion perception as a potential endophenotype for schizophrenia, several critical questions remain that preclude firm conclusions from these findings. Perhaps, most importantly, none of these investigations have evaluated the independence of this finding relative to the well-replicated deficits in neurocognitive functioning seen between unaffected relatives and healthy controls.[12] Although research has supported the notion that social cognition and neurocognition are distinct constructs,[15,21] a clear relationship does exist in individuals with the illness.[15] The extent of this relationship in unaffected relatives is largely unknown, but if present, it is possible that neurocognitive impairment alone could account for the sometimes subtle poorer performance of unaffected relatives on social cognitive tasks. Further, even if social cognitive impairment exists independent of deficits in neurocognition among genetically predisposed samples, little is known about the degree to which these impairments are associated with manifestations of schizophrenia-spectrum symptoms in at-risk samples. Answers to these 2 questions are critical for solidifying social cognitive impairment as a robust and independent endophenotypic marker of schizophrenia.

To begin to address these questions, we conducted a study of social cognitive impairment in relatives of schizophrenia probands and healthy controls to identify the presence of deficits in social cognition, their independence from neurocognitive dysfunction, and their relation to schizophrenia-spectrum psychopathology. Specifically, we aimed to determine whether individuals at familial high risk for schizophrenia would display impairments in social cognition that were independent of neurocognitive dysfunction and, if present, determine whether such impairments would be associated with schizophrenia psychopathology. We hypothesized that at-risk individuals would display impairments in social cognition that were independent of neurocognitive function and that such impairments would be significantly related to prodromal psychopathology portending the development of schizophrenia.

Method

Participants

Participants consisted of 70 first-degree relatives (N = 50; 41 offspring and 9 siblings) and second-degree relatives (N = 20; 12 nieces/nephews, 7 grandchildren, and 1 aunt/uncle) of schizophrenia probands and 63 healthy controls recruited as part of a larger study on the neurobiology and risk for schizophrenia. The participants were identified at the Western Psychiatric Institute and Clinic, Pittsburgh, or related clinical sites. Familial high-risk subjects were recruited by first approaching patients with schizophrenia with eligible relatives in our outpatient clinical services; we also recruited subjects via advertisements in community locations. Subjects were included if they had a first- or second-degree relative with schizophrenia or schizoaffective disorder, had an IQ > 80, did not have any lifetime evidence of a psychotic disorder, had not been exposed to antipsychotic medications, were not abusing substances within the past month or dependent upon substances within the past 6 months, and had no significant neurological or medical conditions. Clinical and neuropsychological characterizations of this sample have been reported elsewhere.[22–25] Age- and gender-matched healthy controls were recruited from the same community neighborhoods as familial high-risk subjects. Sample demographic and clinical characteristics are listed in table 1. Because the majority of the sample consisted of first-degree relatives, most of whom were offspring, and the primary recruitment site for this research was early course and first-episode programs in Pittsburgh, familial high-risk participants recruited for this research were predominantly young. While there were no significant differences between at-risk individuals and healthy controls with regard to demographic characteristics, healthy controls did have significantly greater IQ scores than at-risk individuals.

Measures

Social Cognition. Social cognition was assessed using the Penn Emotion Recognition Test-40, a facial emotion recognition paradigm commonly employed in schizophrenia research.[26] The Penn Emotion Recognition Test-40 is a computer-based test of emotion recognition that randomly presents emotional (happy, sad, angry, or fearful) and nonemotional (neutral) faces to participants

Table 1. Demographic and Clinical Characteristics of the Study Sample

Variable	Control (N = 63) M (SD)/N (%)	High Risk (N = 70) M (SD)/N (%)	Combined (N = 133) M (SD)/N (%)	P^a
Age (y)	16.62 (3.65)	16.30 (3.40)	16.45 (3.51)	.601
Male	24 (38%)	38 (54%)	62 (47%)	.082
Caucasian	41 (65%)	34 (49%)	75 (56%)	.080
Education (y)	10.18 (3.29)	9.72 (3.33)	9.94 (3.31)	.432
IQ	111.27 (13.98)	104.11 (15.02)	107.42 (14.93)	.006
Axis I diagnosis	5 (8%)	38 (58%)	43 (34%)	<.001
Prodromal symptoms				
Positive	—	1.57 (3.42)	—	—
Negative	—	1.86 (3.20)	—	—
Disorganized	—	1.02 (1.73)	—	—
General	—	1.52 (2.57)	—	—
Attenuated positive symptoms[b]	—	7 (10%)	—	—

[a]Fisher Exact test or independent *t* test, 2 tailed, for significant differences between high-risk participants and healthy controls.
[b]Six first-degree relatives and 1 second-degree relative met criteria for prodromal symptoms.

and asks them to choose from the emotional label that best suits the displayed face. A forced-choice format is used during the test where participants have to choose among the labels "happy," "sad," "angry," "fearful," or "neutral" for the face presented. The race and gender of faces are randomly dispersed throughout the task. Key performance metrics from this paradigm include the accuracy with which participants identify emotional and neutral faces, as well as the speed at which participants provide their responses, in the form of reaction time. Previous research has shown this emotion recognition paradigm to be capable of discriminating between schizophrenia patients and healthy controls.[26]

Neurocognition. Neurocognitive data were collected from a neuropsychological battery including the Wechsler Abbreviated Scale of Intelligence[27]; Cogtest Spatial Working Memory Test[28]; Wisconsin Card Sorting Test[29]; the Continuous Performance Test, Identical Pairs version[30]; and a category/letter fluency task[31] to assess IQ, working memory, executive functioning, attention, and verbal fluency, respectively. These particular measures were collected as they represent field standards for assessing the prominent domains of neurocognition impaired in schizophrenia.[1,32] Individual cognitive test scores were extracted from this battery, scaled to a common *z* metric, and averaged to compute an overall composite index of neurocognitive function. Relevant tests were reverse scored so that higher scores reflect better neurocognitive functioning on the composite. Individual test scores included in the composite were the IQ score from the Wechsler Abbreviated Scale of Intelligence, the distance median after a 12-second delay from the Cogtest Spatial Working Memory Test, perseverative

and nonperseverative error scores from the Wisconsin Card Sorting Test, visual *d′* from the Continuous Performance Test, and total correct from the category/letter fluency task. The internal consistency of this composite was within acceptable ranges ($\alpha = .72$).

Prodromal Psychopathology. Prodromal and attenuated positive symptoms were assessed using the Scale of Prodromal Symptoms (SOPS) as part of the Structured Interview for Prodromal Syndromes (SIPS) by trained interviewers.[33] The SIPS is a semistructured interview used to assess prodromal symptoms and states in schizophrenia and related disorders. The SOPS is a 19-item rating scale of the severity of positive, negative, disorganized, and general psychopathology symptoms gleaned during the SIPS interview. Study interviewers were trained using videotapes supplied by Jean Addington, PhD. Interrater reliability for all interviewers was adequate (intraclass correlation coefficient > .70) when examined across 5 videotaped interviews rated by expert raters. Previous research has documented the reliability and validity of SIPS[34,35] and supported the proposed factor structure for the SOPS.[36]

Procedures

Upon recruitment, affected family members were assessed using the Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition)[37] to verify schizophrenia/schizoaffective diagnosis and were screened for inclusion criteria. Eligible participants were then assessed using a comprehensive battery of assessments that included the aforementioned measures of social cognition, neurocognition, and prodromal psychopathology. Missing data were assumed to be missing at random and handled at that time of

Table 2. Emotion Recognition in Individuals at Familial Risk for Schizophrenia and Healthy Controls

Emotion Recognition	Control (N = 63)		High Risk (N = 70)		P^a	d
	M	SD	M	SD		
Accuracy	50.00	10.00	46.72	11.12	.078	−0.31
Emotional faces	50.00	10.00	48.49	10.86	.407	−0.14
Neutral faces	50.00	10.00	45.45	11.59	.017	−0.42
Speed	50.00	10.00	57.60	10.93	<.001	0.73
Emotional faces	50.00	10.00	55.72	10.93	.002	0.55
Neutral faces	50.00	10.00	56.38	10.76	<.001	0.61

Note: Emotion recognition scores are rank transformed due to skewness and standardized to healthy controls with a mean (SD) of 50 (10).
[a]Based on 2-tailed t tests with 131 df.

analysis using the expectation-maximization approach.[38] This research was approved by the University of Pittsburgh Institutional Review Board, and all participants and/or their guardians provided written informed consent prior to participation. For subjects below the age of 18 years, we additionally obtained informed assent.

Results

Do Individuals at Familial High Risk for Schizophrenia Have Deficits in Social Cognition?

We began our investigation of social cognitive impairments in individuals at familial risk for schizophrenia by comparing performance on the emotion recognition paradigm with healthy controls. As can be seen in table 2, while at-risk individuals did not display a deficit in accurately attributing emotions to emotionally laden faces, they were significantly less accurate at correctly attributing emotions to neutral faces, suggesting an overattribution of emotion to neutral facial stimuli. Post hoc analyses of error patterns for individual emotion recognition tasks of neutral faces indicated that most (83%) of the errors made by those at familial high risk for schizophrenia consisted of the overattribution of negative emotions to neutral faces, most commonly (62%) ascribing such faces as sad. With regard to speed during the emotion recognition paradigm, high-risk participants were significantly slower at completing both emotional and neutral face recognition tasks compared with healthy controls (see table 2).

Given that participants at familial risk for schizophrenia also displayed significant cognitive deficits on our neurocognitive composite, $t_{131} = 3.31$, $P = .001$, we proceeded to explore whether these deficits in basic cognition might account for the speed and accuracy deficits observed in the performance of high-risk individuals on the social cognitive emotion recognition tasks. Results from a series of regression models, adjusting for between-group differences in neurocognition by accounting for shared variance with neurocognitive composite

scores, indicated that at-risk participants continued to display significant impairments in accurately completing emotion recognition tasks with neutral faces, $t_{130} = 2.11$, $P = .037$, and continued to perform significantly slower on emotion recognition tasks with emotional, $t_{130} = -2.61$, $P = .010$, and neutral, $t_{130} = -3.17$, $P = .002$, faces even after accounting for their neurocognitive dysfunction. Consequently, while neurocognitive performance was impaired among individuals at familial high risk for schizophrenia, deficits in basic cognition could not account for the performance deficits displayed by these individuals during the social cognitive emotion recognition paradigm.

Are Deficits in Social Cognition Related to Cognitive Function and Clinical Features?

Having found that individuals at familial high risk for schizophrenia displayed significant impairments in social cognition during an emotion recognition paradigm, cross-sectional relations between these impairments and cognitive and clinical outcomes were examined to explore how social cognitive impairments might relate to prodromal psychopathology and neurocognitive functioning. As can be seen in table 3, only the domain of emotion recognition accuracy where high-risk individuals displayed a significant performance deficit (identifying neutral faces) was related to prodromal psychopathology. Specifically, high-risk individuals who performed poorly on the neutral facial identification task displayed significantly greater attenuated positive and general psychopathology symptoms. Increased reaction time during neutral emotion recognition tasks was also significantly associated with prodromal general psychopathology. Further, these relations persisted, even after removing shared variance with age and gender, both of which were modestly associated with emotion recognition performance (mean $|r| = .17$).

Conversely, no significant relations were found between neurocognitive composite scores and positive ($r = -.05$, nonsignificant [ns]), negative ($r = -.10$, ns),

Table 3. Relations Between Emotion Recognition, Clinical, and Cognitive Characteristics Among Individuals at Familial High Risk for Schizophrenia ($N = 70$)

Variable	Emotion Perception					
	Accuracy			Speed		
	Total	Emotional Faces	Neutral Faces	Total	Emotional Faces	Neutral Faces
Prodromal symptoms						
Positive	−.21† (−.30*)	−.03 (−.13)	−.36** (−.39**)	.03 (−.001)	−.08 (−.10)	.20† (.18)
Negative	−.07 (−.12)	−.08 (−.14)	.02 (.01)	−.03 (−.03)	−.05 (−.05)	−.13 (−.13)
Disorganized	−.22† (−.27*)	−.14 (−.21†)	−.002 (−.01)	08 (.06)	.08 (.06)	−.12 (−.14)
General psychopathology	−.0003 (−.21†)	.22† (.05)	−.36** (−.46**)	.24* (.24*)	.14 (.12)	.26* (.26*)
Neurocognition composite	.19 (.11)	.14 (.02)	.06 (.03)	.06 (.01)	−.06 (−.11)	.13 (.09)

Note: Partial correlation analyses adjusting for shared variance with age and gender appearing in parentheses.
†$P < .10$, *$P < .05$, **$P < .01$, 2 tailed.

or general psychopathologic ($r = −.16$, ns) prodromal symptoms. However, neurocognitive function was moderately associated with disorganized symptoms, as one might expect ($r = −.46$, $P < .0001$). Exploratory analyses of the association between individual neurocognitive measures and prodromal symptoms indicated that IQ was the only consistent predictor of all domains of prodromal symptomatology (range of $r = −.58$ to $−.36$, all $P < .01$), particularly disorganized symptoms. In addition, greater perseverative ($r = .30$, $P = .013$) and nonperseverative ($r = .32$, $P = .006$) errors on the Wisconsin Card Sorting Test were significantly related to more positive prodromal symptoms, whereas greater verbal fluency was related to less negative ($r = −.35$, $P = .003$) and disorganized symptoms ($r = −.32$, $P = .007$). Interestingly, greater visual d' scores from the Continuous Performance Test were associated with increased positive ($r = .36$, $P = .002$) and negative ($r = .31$, $P = .009$) prodromal symptoms. No other significant relations between individual neurocognitive tests and prodromal symptoms were observed.

As suggested by our previous regression analyses, neurocognitive functioning as measured by an overall neurocognitive composite index was not significantly related to performance on the social cognitive emotion recognition tasks, indicating a general independence of neurocognitive and social cognitive disability among high-risk individuals (see table 3). Exploratory within-composite analyses of the relationship between individual neurocognitive domains and emotion recognition performance indicated that the only significant relations between emotion recognition and neurocognitive tasks were associations between verbal fluency and overall emotion recognition accuracy ($r = .31$, $P = .009$) and accuracy of recognition of emotional faces ($r = .24$, $P = .048$), and an association between perseverative errors on the Wisconsin Card Sorting Test and reaction time for recogniz-

ing neutral faces ($r = −.25$, $P = .039$). No other significant relations between neurocognitive and emotion recognition tasks were observed.

Discussion

Identifying endophenotypes for schizophrenia among at-risk samples has become a critical area of investigation that has the potential to direct early detection and intervention programs.[39] Neurobiologically based impairments in cognition have been promising candidates for reliable endophenotypes of the disorder.[11] Unfortunately, while individuals who ultimately develop schizophrenia demonstrate significant impairments in both social cognitive and neurocognitive function,[1,40] the majority of research on cognitive risk markers for schizophrenia has focused exclusively on neurocognitive domains. As such, little is known about the degree to which impairments in social cognition are present among individuals at risk for the disorder, beyond the well-documented neurocognitive deficits experienced by the population,[12] or whether such premorbid deficits are associated with the increased prodromal symptoms that can mark the transition to psychosis.

This research investigated the presence of social cognitive impairments in facial emotion recognition among at-risk relatives of patients with schizophrenia and healthy controls. Results indicated that individuals at familial high risk for schizophrenia were significantly more likely to overattribute emotions to neutral faces and predominantly misinterpreted such faces as negatively valenced. This deficit in the emotional interpretation of neutral faces persisted after adjusting for overall deficits in neurocognition and was significantly related to both prodromal positive symptoms and general psychopathology, whereas neurocognitive impairment was only associated with prodromal symptoms of disorganization. In addition,

significant degradations in the speed with which at-risk individuals completed emotion recognition tasks were observed, regardless of the valence of the stimuli, and reduced reaction time in completing neutral facial recognition tasks was significantly associated with increased prodromal general psychopathological symptoms. The observed deficits in processing speed during emotion recognition tasks were also present after adjusting for overall neurocognitive dysfunction.

These findings support a social cognitive deficit in emotion recognition as a potential unique endophenotype and risk marker for schizophrenia. That at-risk individuals tended to show a general overattribution bias toward labeling neutral faces as negative and that this bias was associated with prodromal symptomatology are particularly interesting given theoretical and empirical work on the formation of positive symptoms. For example, prominent models of delusion formation suggest that individuals with persecutory delusions and paranoia are prone to selectively attending to negative stimuli.[16] Such a bias has been proposed as stemming from social cognitive deficits in the processing and interpretation of social stimuli, which has received support from both the interpersonal attribution and theory of mind literature.[41] Further, investigators employing the same emotion recognition paradigm used in this study have shown that patients with chronic schizophrenia also exhibit a negative overattribution bias toward neutral faces,[26] suggesting that negative interpretations of neutral stimuli may be generally characteristic of those with positive symptoms. The findings of this research support these investigations and indicate that such deficits in emotion perception may be an early precursor to the development of positive symptoms and ultimately schizophrenia, as the frequent misinterpretations of benign social stimuli as negative observed in this sample would seem likely to lead to the kind of information processing biases that Bentall et al[16] describe in delusion formation. In addition to contributing to the development of positive symptoms, it seems plausible that the misinterpretation of neutral faces could have sizable functional consequences on social behavior as well. For example, negative displays of affect usually cue individuals to avoid social interaction, and if there is a negative overattribution bias toward even neutral faces, it is likely that significant social withdrawal and avoidance could result, as is common in schizophrenia. Subsequent studies are needed to further examine the predictive strength of these emotion recognition biases to the development of schizophrenia and related disorders in order to determine whether such deficits are truly early prognostic markers of those who will develop positive symptomatology and psychosis.

It is also interesting that the social cognitive and neurocognitive measures used in this research were largely independent. As discussed above, social cognitive deficits in the perception of neutral faces all persisted after adjusting for a significant neurocognitive performance deficit. Further, emotion recognition and individual neurocognitive measures showed few significant relations, and all were small in magnitude.[42] Such findings largely support research with patients with schizophrenia indicating that neurocognitive and social cognitive impairments appear to be separate but related constructs, both of which warrant investigation.[15,43] The absence of more sizable relations with neurocognitive function in this at-risk sample may be specific to either this population or the measure of emotion recognition used. It is possible that emotion recognition and general cognitive impairments may become more closely related as the phenotype of schizophrenia emerges, as studies of patients with chronic schizophrenia using similar measures have shown stronger relations between these constructs.[44] Unfortunately, to date, few studies have examined social cognitive impairments as potential endophenotypes and risk markers for schizophrenia in at-risk samples, and to our knowledge, no investigation has examined both neurocognitive and social cognitive impairments within a single study. Clearly more work in this area is needed, as a number of deficits in social cognition beyond emotion recognition have been documented in schizophrenia.[40] However, the degree to which deficits beyond emotion recognition are present in at-risk samples or uniquely predictive of the development of schizophrenia is largely unknown. Subsequent studies will need to broaden social cognitive assessment to additional domains, such as perspective taking, emotion management, interpersonal attribution, and theory of mind and employ longitudinal designs to examine the stability and predictive utility of deficits in these areas.

Finally, it is important to note that while this research suggests that social cognitive impairments in emotion recognition may be a potential endophenotype for schizophrenia, several limitations preclude firm conclusions regarding the endophenotypic status of such deficits. To begin, this investigation was not able to reliably examine heritability estimates across individuals with different genetic loadings for schizophrenia (eg, multiplex vs simplex families, first-degree vs second-degree relatives) due to its modest sample size and primary inclusion of first-degree relatives. In addition, the use of a single measure of emotion recognition to assess social cognition makes it difficult to determine whether broad impairments in other social cognitive domains (eg, perspective taking, social cue recognition, emotion regulation) exist in at-risk relatives or whether impairments are circumscribed to emotion recognition. The young sample of at-risk relatives studied in this research also indicates a need for further study as these individuals age and with older at-risk samples in order to identify the generalizability of these findings to older individuals. Continued exploration of these deficits among individuals at clinical high risk for the disorder, as done by Addington et al,[45] will be particularly important in future studies, as

this study focused only on individuals at familial risk for the disorder, few of whom met clinical high-risk criteria. In addition, this cross-sectional study provides no information about the stability or predictive power of social cognitive deficits toward schizophrenia development in at-risk samples. Further, familial high-risk and healthy control individuals were not matched in this research for IQ, although analyses adjusting for differences in neurocognitive ability (which included IQ) suggested that the impairments in social cognition seen in at-risk relatives cannot be accounted for by a general neurocognitive deficit. Finally, the degree to which these deficits are unique to individuals who will develop schizophrenia vs those who develop another disorder remains unanswered. Rather, by showing an increased prevalence of this deficit in unaffected individuals, our data represent a first step in this regard.

Carefully designed family studies with adequate numbers of individuals with diverse ages and different genetic loadings for schizophrenia that incorporate longitudinal designs, other psychiatric populations, broader measures of social cognition, and both molecular and neurobiologic measures are needed to verify the potential of social cognitive deficits as true endophenotypes for schizophrenia. Such studies are likely to not only provide critical information about the pathophysiology of the disorder but also point to promising directions for early intervention and prevention programs. Our recent work with cognitive enhancement therapy,[46] a social and nonsocial cognitive rehabilitation approach for schizophrenia, has already yielded very promising preliminary results when applied early in the illness.[47] If social cognitive impairments are strong precursors to schizophrenia development, the application of such approaches as cognitive enhancement therapy to at-risk individuals may be particularly effective for altering the deteriorative course of the disorder.

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