The Course of Neurocognition and Social Functioning in Individuals at Ultra High Risk for Psychosis

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Objective: This study evaluates longitudinal neuropsychological performance and its association with clinical symptomatology and psychosocial outcome in individuals identified as ultra high risk (UHR) for psychosis. Methods: Thirty-five UHR individuals completed neurocognitive, clinical, and social/role functioning assessments at baseline and, on average, 8.3 months later. Results: UHR subjects showed significant cognitive deficits at baseline and 2 distinct profiles of cognitive change over time. On average, 50% demonstrated improvement in social and role functioning over the follow-up period, while the other half showed either stability or decline in functioning. Functional improvement was associated with improved processing speed and visual memory, as well as improvement in clinical symptoms over the follow-up period. In contrast, patients who did not improve functionally showed stable clinical symptoms and cognitive performance over time. Conclusions: Although the degree of neurocognitive deficit at baseline in UHR patients does not predict psychosocial outcome, the course of neurocognitive change over the first 8 months of follow-up does differentiate patients with good and poor functional outcomes.

Key words: prodrome/cognition/high risk/social functioning/functional outcome/psychosis

The prodromal phase of schizophrenia is hypothesized to represent a period of progressive cognitive and functional deterioration coincident with emergence of subthreshold psychotic symptoms. While most individuals with schizophrenia experience onset during late adulthood, deficits in cognition are evident years before the development of psychotic symptoms, during childhood and adolescence.1–5 These cognitive deficits are hypothesized to accelerate during the prodromal period in association with changes in brain functioning that may lead to the development of psychotic symptoms6,7 as well as functional decline in a variety of domains.8

Recent studies have shown that individuals thought to be at ultra high risk (UHR) for developing psychosis demonstrate neuropsychological deficits that are associated with poor social and role functioning. Dysfunction in multiple cognitive domains has been reported in investigations of UHR samples,8–18 with the most pronounced deficits observed on measures of visual attention and working memory, processing speed, verbal learning and memory, and executive functioning, including measures of verbal fluency and set shifting. In addition, we recently demonstrated that deficits in verbal learning and memory are predictive of current social functioning in UHR individuals, irrespective of negative or positive symptom severity.18 UHR individuals do not show the level of cognitive impairment reported in studies of patients with first-episode6,10,13,15 or chronic schizophrenia,15 and such differences in cognitive performance between UHR and first-episode subjects suggest a dynamic change in cognitive processes in the period prior to psychosis onset. However, very little empirical evidence is available to address this question,19 and it remains unclear whether any deterioration that does occur is specific to the prodromal period.

While these studies of UHR individuals confirm that neuropsychological deficits and functional impairment are detectable before the onset of psychosis, such investigations do not account for the clinical heterogeneity that exists within UHR populations. As described by Yung and colleagues,20 UHR populations are a mixture of 3 subgroups: at-risk individuals who will subsequently develop psychosis (true positives); at-risk individuals who do not transition to psychosis because of resiliency, treatment, or protective factors (false false positives); and those individuals whose at-risk state actually represents a vulnerability for another type of psychological disorder with a different underlying pathology (true false positives).

As a result of this inherent clinical heterogeneity, UHR studies have begun to examine change in clinical
symptoms and cognitive performance over follow-up periods with the hope of identifying those individuals at highest risk for subsequent conversion to psychosis. While a few studies have highlighted a pattern of greater baseline cognitive impairment that is associated with subsequent conversion,\textsuperscript{8,9,16} no study to date has examined the effects of cognitive and clinical change on psychosocial functioning in UHR individuals.

Thus, we sought to explore potential aspects associated with the previously delineated UHR subgroups by investigating the interrelated patterns of change in cognition, clinical symptoms, and functioning that may occur for UHR individuals over the critical period following ascertainment. Specifically, we chose to focus on predictors of subsequent psychosocial functioning, rather than conversion to psychosis, in order to understand factors associated with impairment in social and role functioning at follow-up independent of final diagnostic outcome. Based on previous findings in UHR\textsuperscript{8–18} and first-episode samples,\textsuperscript{21} we predicted that a subgroup of UHR individuals would show baseline cognitive deficits and that such deficits would be associated with severity of negative symptoms as well as poorer role and social functioning, independent of positive symptom severity, at follow-up. Furthermore, we hypothesized that this subset of UHR individuals would show deterioration in cognitive performance over the follow-up period and that such decline would be associated with the deterioration in clinical and functional status thought to predate the onset of psychosis.

Methods

Participants

Participants in this study are part of a larger longitudinal prospective study of adolescents and young adults enrolled in research at the Center for the Assessment and Prevention of Prodromal States (CAPPS) at the University of California, Los Angeles (UCLA). Eligible individuals must be between the ages of 12 and 35 years and have reasonable fluency in English to allow valid, standardized application of the assessment instruments. Participants also must meet criteria for 1 of the 3 prodromal syndromes, as assessed by the Structured Interview for Prodromal Syndromes (SIPS\textsuperscript{22}), based on presence of (1) attenuated psychotic symptoms (Attenuated Positive Symptom Syndrome); (2) transient psychotic symptoms (Brief Intermittent Psychotic Syndrome, BIPS); or (3) a substantial drop in social/role functioning in conjunction with schizotypal personality disorder diagnosis or presence of psychotic disorder in first-degree relative (Genetic Risk & Deterioration Syndrome). For cases in which the frequency of psychotic symptoms was difficult to determine, such individuals were included within the BIPS category if their psychotic symptoms began within the past 3 months and they did not meet criteria for a schizophrenia-spectrum diagnosis.

At baseline, adolescents aged 15 and older also completed the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV, Axis I Disorders\textsuperscript{23} while participants 14 years and younger were administered the Kiddie Schedule for Affective Disorders and Schizophrenia\textsuperscript{24,25}. Participants were excluded from the study if they met DSM-IV criteria for an Axis I schizophrenia-spectrum diagnosis, such as schizophrenia, schizoaffective disorder, schizophreniform disorder, or delusional disorder.\textsuperscript{26} Additional exclusion criteria include the presence of a neurological disorder, DSM-IV diagnosis of drug or alcohol abuse or dependence, and/or IQ below 70. For individuals with a Wechsler Abbreviated Scale of Intelligence (WASI\textsuperscript{27}) estimated IQ less than or equal to 70, Full Scale IQ was determined by a complete WISC-III/WAIS-III assessment by a qualified CAPPS examiner or recent previous assessment by a qualified professional. Detailed information regarding SIPS prodromal criteria, interrater reliability, and case consensus procedures have been described in detail elsewhere.\textsuperscript{30}

The participants completed informed consent or assent for the intake screening and were compensated for their participation in all assessments. Parental informed consent for minors was also obtained. Study protocol and informed consent procedures were approved by the UCLA Institutional Review Board.

Demographic data for UHR individuals included in these analyses (n = 35) are shown in Table 1. Eighty percent of study participants received psychotropic medication as part of their usual care at baseline, and 89% were taking at least 1 medication at follow-up. These medications included atypical antipsychotic medications (49% at baseline, 51% at follow-up), mood stabilizers (17%, 23%), and SSRI antidepressants (34%, 40%). Over the follow-up period, participants also received a variety of psychosocial treatments that were provided in an unstructured format by both CAPPS and community treatment providers. These treatments included individual psychotherapy (83%), family therapy (34%), group therapy (37%), and school-based therapy or counseling (57%). Seventy-four percent of the participants received 2 or more forms of psychotherapy (eg, individual therapy plus group therapy) over the follow-up period. Ninety-seven percent of the participants also received case management services from a CAPPS staff member.

Procedures

In the SIPS interview,\textsuperscript{22,31} symptoms are rated on 4 main scales of the Scale of Prodromal Symptoms (SOPS): positive, negative, disorganized, and general symptoms. To reduce the number of statistical comparisons, our hypotheses in the current investigation focus on the positive
and negative symptom scales. The SOPS Positive Symptom Scale assesses symptoms related to unusual thought content, suspiciousness, perceptual disturbances/hallucinations, grandiosity, and disorganized communication. Symptoms of anhedonia, avolition, flat affect, decreased role functioning, and decreased verbal comprehension/abstraction are captured by the SOPS Negative Symptom Scale. A Global Assessment of Functioning score, revised for use with the SIPS, is also administered at intake.

At the time of the baseline interview, social and role functioning were assessed with the Global Functioning: Social Scale (GF:Social), the Global Functioning: Role Scale score, mean (±SD), [range] Baseline 5.60 (1.68), [2–9] Follow-up 6.09 (1.58), [2–9]
The GF:Social and GF:Role scales provide ratings of functioning in both social and role domains on 2 separate 10-point Likert scales, which are scored independently of symptom severity. The GF:Social and GF:Role scales are 2 new measures (see Cornblatt et al [2007], this issue) that are designed to provide a global measure of psychosocial functioning in younger populations. The SCOS contains three 4-point items assessing duration and frequency of hospitalizations, social contacts with individuals outside of the family, and useful employment or participation in school. The SAS contains seven 5-point items evaluating peer and romantic relationships and participation in activities and organizations. Scores for each item on the SCOS and SAS were summed into 1 total score for each measure. Ratings for all scales described were based on the past month.

A comprehensive neuropsychological examination assessing multiple domains of cognitive functioning (Table 2) was also administered at baseline and follow-up by supervised clinical psychology doctoral students or PhD staff. Participants were assessed with age-appropriate forms for specific cognitive measures, when statistically comparable versions were available, and raw scores were converted to age-matched scaled scores before z score transformation was completed using published normative data. In order to reduce the number of statistical comparisons, the measures were combined into 5 dimensions of cognitive functioning (processing speed, reasoning and problem solving, visual learning and memory, verbal working memory, and verbal learning and memory) that have been identified as domains of impairment in patients with schizophrenia. In addition, a measure assessing the domain of motor speed was included in the battery.

**Statistical Analysis**

The demographic variables of age, gender, handedness, and parental education were examined to determine if these variables showed a significant relationship to WASIQ at baseline. Preliminary analyses revealed that participants’ estimated WASIQ at baseline did not differ based on gender [40% female; F(1, 34) = 0.32, P = .58], handedness [89% right-handed; F(1, 34) = 0.89, P = .35] or parental education [58% college educated; F(6, 32) = 2.24, P = .07]. Participants’ age was not significantly correlated with WASIQ (r = 0.18, P = .29) or performance on the 6 cognitive domains at either baseline or follow-up.

To analyze the nature and severity of cognitive deficits at baseline and follow-up, UHR participants’ average performance within the 6 cognitive domains (speed of processing, working memory, verbal learning and memory, visual learning and memory, reasoning and problem solving, and motor speed) from baseline to follow-up was analyzed in a paired-samples t test. Independent-samples t tests were used to analyze differences in the baseline cognitive performance of individuals who demonstrated improvement in functioning by follow-up when compared with those who remained stable.

### Table 2. Neuropsychological Measures and Published Normative Data

<table>
<thead>
<tr>
<th>Cognitive Domain</th>
<th>Test Used</th>
<th>Norms Used in z Score Transformation</th>
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</thead>
<tbody>
<tr>
<td>Processing speed</td>
<td>Trail-Making Test A and B63</td>
<td>Trail-Making Test: ages 12–144; ages 15–39</td>
</tr>
<tr>
<td></td>
<td>WISC-III/WAIS-III Digit Symbol Coding</td>
<td>Digit Symbol Coding: ages 12–15, WISC-III57; ages 16+, WAIS-III58</td>
</tr>
<tr>
<td>Reasoning and problem solving</td>
<td>WASI Matrix Reasoning</td>
<td>WASI54</td>
</tr>
<tr>
<td>Visual learning and memory</td>
<td>WMS-III Visual Reproduction Immediate and Delayed Recall</td>
<td>WISC-III57, WAIS-III58</td>
</tr>
<tr>
<td>Verbal working memory</td>
<td>WISC-III/WAIS-III Digit Span Backward</td>
<td>CVLT-II/CVLT-C 1–5 Total</td>
</tr>
<tr>
<td>Verbal learning and memory</td>
<td>CMS Stories/WMS-III Logical Memory Immediate and Delayed Recall</td>
<td>Ages 12–15: CMS71; ages 16+: WMS-III68</td>
</tr>
<tr>
<td>Motor speed</td>
<td>Finger Tapping Test, Average of dominant and nondominant hand scores</td>
<td>Ages 12–156; Ages 15–3972</td>
</tr>
</tbody>
</table>

Note: WISC-III, Wechsler Intelligence Scale for Children-III; WAIS-III, Wechsler Adult Intelligence Scale-III; WASI, Wechsler Abbreviated Scale of Intelligence; CVLT-II, California Verbal Learning Test-II; CVLT-C, California Verbal Learning Test—Children’s Edition Trials; CMS, Children’s Memory Scale; WMS-III, Wechsler Memory Scale-III.
or declined in functioning. In concordance with the standard level of change considered to be clinically significant in clinical trials, improvement in functioning was defined as a 20% or greater increase from the baseline functioning score on the SCOS, SAS, GF:Social, or GF:Role functioning scales. Group differences in performance on the 6 cognitive domains and SOPS Positive and Negative Symptom Total scores at baseline were examined using independent t tests for each of the functioning measures.

To address the relationship between change in cognitive performance and change in functioning over the follow-up period, independent-samples t tests were used to examine differences in the profile of cognitive change scores for individuals who demonstrated 20% improvement in functioning by follow-up when compared with those who remained stable or declined. To create cognitive change scores, UHR participants’ baseline performance on each of the 6 cognitive domains was subtracted from their follow-up performance, so that a positive change score reflected improvement in cognitive functioning for that domain. Similarly, change in social/role functioning was determined by subtracting the baseline total score from the follow-up total score on each of the 4 functioning measures, so that a positive functioning change score reflected improvement in social or role functioning. In contrast, change scores for SOPS positive and negative symptoms were created by subtracting follow-up presentation from baseline severity, such that a positive symptom change score reflected a decrease in symptom severity. Post hoc analyses addressed potential confounding variables, such as the potential effects of family history of psychotic illness, presence of schizotypal personality disorder, use of antipsychotic medications, and participation in psychosocial treatment.

All analyses were univariate and 2-tailed with alpha set at P ≤ .05 to allow for recognition of smaller effects due to small sample size and possible power limitations. This exploratory approach sought to generate hypotheses for future studies and encourage additional work in this area of research.

Results

Compared with published normative samples, UHR participants’ baseline performance revealed significant deficits in speed of processing (t = −3.59(33), P = .001) and motor speed (t = −3.27(33), P = .003), with a trend toward impaired verbal learning and memory (t = −1.82(31), P = .08). As shown in Figure 1, participants showed significant improvement, on average, over the follow-up period in the domains of processing speed (t = −3.56(33), P = .001), verbal learning and memory (t = −4.11(30), P < .001), visual learning and memory (t = −2.52(19), P = .02), and motor speed (t = −2.39(32), P = .02). Participants did not show significant change in performance on measures of verbal working memory (t = −1.13(34), P = .27) or reasoning and problem solving (t = −1.42(34), P = .17).

On average, 50% of UHR individuals evidenced improvement in social and/or role functioning over the follow-up period, with 37%–43% showing a 20% or greater increase from their baseline functioning scores. Low to moderate associations were observed between the baseline and follow-up scores on each of the 4 functioning measures (SAS r = 0.63, P ≤ .001; SCOS r = 0.25, P = .15; GF:Social r = 0.49, P = .003; GF:Role r = 0.51, P = .002), providing further evidence for a lack of stability in participants’ social and role functioning over time.

There were no significant relationships between baseline cognitive functioning and level of clinical symptoms or social/role functioning at follow-up. However, the rates of improvement in symptoms and cognitive functioning

Fig. 1. Change in Patients’ Mean Performance (± score ± SEM) on 6 Cognitive Domains Between Baseline and Follow-up.
differentiated those UHR individuals who improved functionally from those who did not. As shown in Figure 2, a 20% or greater improvement in baseline GF:Social functioning was associated with significant improvement in processing speed \( t = -2.26(32), P = .03 \) and Visual Learning and Memory \( t = -2.56(18), P = .02 \) as individuals who improved in social functioning also showed improved processing speed [change mean \( z \) score (SD) = 0.73 (0.53)] and visual learning and memory [change mean \( z \) score (SD) = 1.22 (1.07)] over the follow-up period when compared with those individuals who did not show improvement on the GF:Social [processing speed change mean \( z \) score (SD) = 0.20 (0.77); visual learning change mean \( z \) score (SD) = 0.21 (0.68)]. Additionally, a 20% or greater improvement in SAS Total Score was associated with differential change in SOPS Positive Symptom Score \( t = 2.43(32), P = .02 \) because individuals who improved on the SAS showed a larger decrease in positive symptomatology [positive symptom change mean \( z \) score (SD) = 6.62 (4.03)] than those individuals who did not show improvement in social functioning according to the SAS [positive symptom change mean \( z \) score (SD) = 2.76 (4.75)].

Finally, a 20% or greater improvement in role functioning, according to SCOS total score, was significantly associated with change in the SOPS Negative Symptom Total Score \( t = 3.26(24.56), P = .003 \) and SOPS Positive Symptom Total Score \( t = 2.24(32), P = .03 \) because those individuals who showed functional improvement also showed a larger decline in negative [negative symptom change mean \( z \) score (SD) = 6.07 (2.81)] and positive symptoms [positive symptom change mean \( z \) score (SD) = 5.93 (3.39)] when compared with those who did not improve on the SCOS [negative symptom change mean \( z \) score (SD) = -0.40 (8.24); positive symptom change mean \( z \) score (SD) = 2.55 (5.49)].

Post hoc analyses of possible confounding factors revealed no significant effect of family history of psychotic illness, diagnosis of schizotypal personality disorder, or use of antipsychotic medication on cognition, clinical symptoms, or social/role functioning. While participation in psychotherapy was not associated with change in cognition or social/role functioning, participation in 2 or more forms of psychosocial treatment during the follow-up period was significantly associated with a 20% decline in SOPS positive symptoms \( \chi^2 = 6.41, P = .04 \).

**Discussion**

This study confirms the presence of baseline neuropsychological deficits in individuals at UHR for psychosis and provides the first evidence of longitudinal associations between neuropsychological functioning, clinical symptomatology, and social/role functioning in this population. At baseline, UHR individuals demonstrated a pattern of deficit in measures of speeded information processing, with a trend toward impaired verbal learning and memory. This profile is similar to that observed in
other UHR samples as well as individuals with established psychotic illness, lending support to the notion that individuals showing emerging clinical signs of illness are on a continuum with fully psychotic individuals.

Additionally, this investigation is one of the first to demonstrate that a subset of UHR individuals show a pattern of improvement in multiple cognitive domains, specifically processing speed, verbal and visual learning and memory, and motor speed at follow-up approximately 8 months later. Although there is some evidence for short-term improvement in some cognitive domains in first-episode schizophrenia as a result of pharmacological interventions, the overall degree of cognitive impairment appears relatively stable across the lifetime course of the illness. The current findings suggest that the pattern of cognitive deficits observed at baseline in a subset of putatively prodromal individuals may reflect difficulties associated with generalized psychiatric distress, as opposed to a stable, underlying trait specifically associated with risk for psychosis. Therefore, some UHR individuals share certain phenotypic features with those who progress to psychosis, but possibly for different underlying reasons.

Additionally, results of the current study revealed that UHR individuals’ functional improvement at follow-up was not predicted by their cognitive performance at baseline, but functional improvement was associated with improvement in both cognition and clinical symptoms over the follow-up period. In other words, those individuals who showed improvement in social or role functioning over the follow-up period also had improved cognitive performance and decreased symptoms over time. Specifically, improvement in social functioning was associated with significant improvement in both processing speed and visual learning and memory at follow-up. Given that UHR participants in this sample show significant cognitive improvement in many domains, these findings reveal that it may be this pattern of change in cognition over the follow-up period, rather than severity of cognitive deficits at baseline, that is related to improvement in functioning over time.

Furthermore, results showed that improvement in social functioning was associated with a larger decrease in positive symptoms over the follow-up period, suggesting that acute symptomatology may play a stronger role in social functioning in UHR patients than is observed for patients with full-blown psychosis. Likewise, improvement in role functioning was associated with a larger decrease in negative symptoms over time, lending support to the notion that negative symptoms have a notable impact on role functioning in UHR individuals.

Several possible alternative explanations for the pattern of cognitive improvement observed in this study bear consideration. In particular, practice effects and the effects of interventions may arguably play a role. Research shows improved functional outcome with earlier intervention in the treatment of psychotic disorders and many of the study participants received some form of psychiatric or psychological treatment during the course of the study. Such treatment is ethically necessary due to the participants’ level of distress and functional impairment, but these interventions likely affect the natural course of the disorder and contribute to clinical and functional improvement. In the current study, participants who received 2 or more types of psychotherapy over the follow-up period were significantly more likely to show a 20% decrease in positive symptoms, suggesting that psychosocial interventions may have a strong impact on clinical distress in this at-risk population. However, such treatment was not associated with changes in cognitive or psychosocial functioning. Unfortunately, sample size and the high percentage of study participants receiving treatment prohibited comparison of individuals receiving vs those who declined treatment and between individuals receiving different forms of treatment. Nevertheless, longitudinal analyses of patients with schizophrenia typically show a pattern of stable cognitive functioning across the lifespan course of illness, despite improvement in psychotic symptom severity in response to psychosocial treatment, which is in contrast to the pattern of cognitive, clinical, and functional improvement observed here. In order to address these issues definitively, future studies will need to use matched non-UHR samples to control for practice effects, as well as UHR individuals receiving alternative types of treatment to examine the effects of psychotherapy and medication on cognition and social/role functioning.

Although one also could hypothesize that these findings of improvement were driven by the subset of “false positives” within this sample, additional analyses revealed that individuals who subsequently converted to psychotic disorder diagnoses (“true positives,” n = 9, 25% of the sample) showed the same patterns of baseline cognitive deficits and subsequent improvement in cognition, clinical symptoms, and functioning when compared with those who did not convert. Consistent with some recent findings in first-episode treatment studies using novel atypical antipsychotic compounds, these results suggest that early intervention may attenuate the effects of psychosis on cognition and contribute to better outcome, even for those who subsequently develop a psychotic disorder.

Many researchers have highlighted the potential of cognitive dysfunction as a possible latent marker, or endophenotype, of genetic risk for schizophrenia. While the current findings provide evidence supporting the growing body of research on the presence of cognitive deficits in individuals at high risk for developing psychosis, the pattern of cognitive improvement observed in this study encourages critical examination of the potential utility of baseline cognitive deficits as definitive markers for heightened risk for psychotic illness in a clinical high-risk sample. The observation of improvement in multiple
cognitive domains in association with clinical and functional improvement suggests that baseline cognitive deficits in a subgroup of UHR individuals may represent a state-specific factor, associated with diffuse psychological distress and poor functioning, which may affect cognitive performance independent of final diagnostic outcome. Alternatively, the pattern of deficits observed here could represent an interaction between psychological state at ascertainment and underlying trait factors that are associated with risk for psychosis or other psychiatric disorders. These competing explanations warrant further investigation in future studies.

A previous analysis\textsuperscript{30} of DSM-IV diagnoses in this sample revealed that many of the UHR participants met criteria for a mood or anxiety disorder diagnosis at ascertainment, diagnoses which other studies\textsuperscript{61–63} have found to be associated with cognitive impairment in the domains observed here. Given that UHR populations are a mixture of true and false positives, the cognitive deficits observed in UHR samples at ascertainment may represent the manifestation of impairment associated with generalized risk for a variety of psychological disorders rather than a vulnerability that is specific to psychosis. Therefore, the results of this study suggest that the pattern of change in cognition and functioning over time may provide a more accurate means of separating the false positives, who show improvement in state-related deficits over time, from the true positives, who show more stable trait-like deficits representing endophenotypic markers of underlying risk.

Therefore, these findings provide novel evidence suggesting that individuals identified as UHR are not predestined to a path of psychological, cognitive, and functional decline. To the contrary, the demonstration of improvement in multiple cognitive domains highlights the power of early identification and intervention in this at-risk population. Overall, the results of this study suggest that UHR individuals should be examined over time because it may be the pattern of cognitive and symptom change or stability that may differentiate those individuals who are at highest risk for further psychological deterioration.

While this study offers support for early identification as a means of improving functional outcome, results should be interpreted with caution due to the small sample size. These findings provide the first glimpse into relationships between cognition, symptoms, and functioning over time and are presented to generate hypotheses and encourage future research in this area. However, it should be noted that the lack of statistical power may have reduced the ability to detect differences between the groups. Additionally, small sample size precluded the investigation of the different patterns of association between cognitive, clinical, and social/role functioning measures presented in the current study. Further analyses should be pursued in larger samples to validate these findings, examine specificity of deficits observed here, and uncover additional relationships that may have been obscured in the current analysis.

As noted previously, this current study is limited by its lack of a normal comparison group and resulting use of published normative data for comparison to this clinical sample. However, such published normal samples were developed and published in order to provide adequate comparisons for clinical data. Given the difficulty in obtaining well-matched adolescent control samples, researchers commonly utilize such published norms.\textsuperscript{15} Nonetheless, comparison to a demographically matched control sample, assessed at similar time points, would strengthen the current findings and should be a priority for future studies. As a related issue, this investigation relied exclusively on standard clinical neuropsychological tests of the domains of cognition sampled, and it is possible that deficits in other domains, such as working memory, would have been observed had we employed experimental paradigms designed to isolate particular aspects of these functions.

Finally, it is important to note that some proportion of individuals within this sample will not progress to develop a diagnosable psychotic disorder, and these individuals would consequently be labeled false positives. As noted previously, the inclusion of such false positives in the group analyses may obscure the presence of significant cognitive deficits in some of the hypothesized domains, and the relationship between such deficits and functional outcome, that may be present if only true positives were examined. Although additional analyses suggested that the pattern of improvement was also characteristic of a small sample of true positives, longitudinal follow-up in larger samples is needed to determine the pattern of neurocognitive, symptomatic, and functional change most predictive of conversion to a full-blown psychotic disorder and to elucidate the complex relationship between such cognitive change, clinical severity, and functional outcome over time.

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