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# Longitudinal changes in social cognition in individuals at clinical high risk for psychosis: An outcome based analysis.

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### Abstract

#### Conflict of Interest

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Drs. Addington, Cannon, Cadenhead, Cornblatt, McGlashan, Perkins, Seidman, Tsuang, Woods, Walker, Mathalon, and Bearden were responsible for the design of the study and for the supervisions of all aspects of data collection. Dr. Shakeel and Ms. Liu were responsible for the statistical analyses. Dr. Shakeel wrote the initial manuscript. Dr. Addington was involved in writing the subsequent drafts of the manuscript. All authors listed were involved in the study design and have contributed to and approved the final manuscript.

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There are no conflicts of interest for any of the authors with respect to the data in this paper or for the study.

Social cognition deficits have been observed in individuals at clinical high risk (CHR) for psychosis. Longitudinal change in social cognition were analyzed in CHR individuals from the North American Prodrome Longitudinal Study (NAPLS2) based on outcome at 24 months. Individuals (*n*=359) were classified into remission, symptomatic, prodromal progression and transition to psychosis (CHR-T) groups. Social cognition was assessed using theory of mind, emotion perception, and social perception tasks. There were no differences at baseline or 24 months between the groups on social cognition. Non-transition groups improved significantly over time on social cognition, but CHR-T did not show this effect.

#### Keywords

Social cognition; Theory of Mind; Social perception; Emotion perception; Clinical high risk; Psychosis

#### 1. Introduction

Social cognition refers to the mental operations that underlie social interactions. Domains of social cognition include theory of mind (ToM) (the ability to attribute beliefs and intentions to oneself and others), emotion perception (the ability to recognize emotions from non-verbal cues), and social perception (the ability to understand social situations) (Pinkham et al., 2014). Social cognition deficits have been well-established in schizophrenia and result in poor real-world functioning (Javed and Charles, 2018). Social cognition has also been investigated in individuals at clinical high risk (CHR) for psychosis, albeit with inconsistent results. While some studies have observed deficits in ToM, emotion perception, and social perception (Green et al., 2012; Kohler et al., 2014), others have not (Brüne et al., 2011; Gee et al., 2012; Stanford et al., 2011). Furthermore, there is no consensus in the literature on whether social cognition deficits can predict conversion to psychosis in CHR (Kim et al., 2011; Piskulic et al., 2016).

Studies that have examined social cognition in CHR are often limited by sample size, absence of longitudinal design, and failure to assess multiple facets of social cognition. They are also limited in considering CHR a homogeneous group. Although some CHR individuals do go on to develop psychosis, others have remission of symptoms, or remain in the at-risk state for years (Tor et al., 2017).

In earlier publications with the North American Prodrome Longitudinal Study (NAPLS-2) sample, we demonstrated that CHR participants perform worse than healthy controls (HC) on several measures of social cognition at baseline (Barbato et al., 2015) and at 12-month and 24-month follow ups (Piskulic et al., 2016). In this study, we aimed to investigate whether longitudinal changes in social cognition are affected by outcome group. We hypothesized that outcome groups with greater severity of symptoms at 24 months will perform worse than other outcome groups on baseline social cognition.

#### 2. Methods

#### 2.1. Participants

Participants for the current study consisted of CHR individuals who were recruited as part of the multi-site NIMH funded NAPLS2 project (Addington et al., 2012). Data were collected from the eight NAPLS sites. Participants were excluded if they met criteria for any Axis I psychotic disorder, had an IQ below 70, or had a history of clinically significant central nervous system disorder. Detailed description of the sample is provided elsewhere (Addington et al., 2015).

Based on their outcome at 24 months, CHR participants were classified as: being in remission if they rated 2 or less on all five positive symptoms (as assessed by the Scale of Prodromal Symptoms (SOPS)); symptomatic if they did not meet current at-risk criteria but continued to rate 3–5 on any one of the five positive symptoms; prodromal progression if they continued to meet at-risk criteria at 24 months; and transition (CHR-T) if they met the criteria for a psychotic disorder during the follow-up period (for details and additional criteria, see Addington et al., 2015).

#### 2.2. Measures

*Structured Interview for Psychosis-risk Syndrome* (SIPS) (McGlashan et al., **2010)** : The SIPS was used to determine whether participants met criteria for being at CHR for psychosis. The SOPS consists of 19 items and rates the severity of CHR symptoms in 4 domains (positive, negative, general, and disorganized symptoms).

**The Awareness of Social Inference Test (TASIT; McDonald et al., 2003):** To assess ToM, the Social Inference subscale of the TASIT was used. TASIT includes 16 short video scenes. In half the scenes, the speaker says something they do not believe (lie) and in the others they say the opposite of what they mean (sarcasm). The participant has to watch the videos and then answer questions about what the characters are doing, thinking, feeling, or saying. TASIT has good psychometric properties and high ecological validity (McDonald et al., 2006, 2004). The total score was used for the present analysis.

**Penn Emotion Recognition (ERT) and Emotion Differentiation Task (EDT; Gur et al., 2002):** To assess facial emotion perception, ERT and EDT were used. In ERT, pictures of faces are shown and the participant has to decide which emotion is represented (anger, fear, neutral, happy, or sad). In EDT, two pictures of faces are shown and the participant has to determine which one shows an emotion (happiness or sadness) more intensely. Total scores on ERT and EDT were used for the present analysis.

**Relationship Across Domains (RAD; Sergi et al., 2009):** To assess social perception, the abbreviated version of RAD was used. RAD contains 15 vignettes which depicts characters following one of four relationship models. Communal sharing represents the idea that individuals are equivalent and undifferentiated, authority ranking represents a hierarchy between individuals, equality matching represents a one-to-one distribution of resources and efforts, and market pricing represents the idea that rewards are proportional to

relative contribution. Each vignette is followed by three statements describing the same characters in a different situation and the participant has to determine which of the relationship models they will follow. The total score was used for the present analysis.

#### 2.3. Procedure

The groups were compared on social cognition at baseline and 24 months. Eighty-six CHR participants transitioned to psychosis in the 2-year period. Follow-up social cognition assessments were collected from CHR-T after they met criteria for a psychotic disorder. For all other groups follow-up social cognition data were collected at 24 months. We have used the term 24 months to refer to the post-transition assessment for CHR-T as well as the 24-month assessment for the remission, symptomatic, and prodromal progression groups (CHR-NT).

#### 2.4. Data Analysis

In order to account for missing data at follow-up assessments and intra-participant correlation over time, Generalized Linear Mixed Model (GLMM) for repeated measures was used to assess longitudinal changes in social cognition between groups with outcome group (remission, symptomatic, prodromal progression, CHR-T) as the independent variable and social cognition task (TASIT, RAD, ERT, EDT) as the dependent variable.

#### 3. Results

The CHR participants were predominantly male (57.1%), white (62.6%), single (94.2%), and students (81.8%). Table 1 shows the result of GLMM for repeated measures between the CHR groups on social cognition. There were no differences at baseline or at 24 months between the groups on the social cognition tasks. However, there was an effect for time within the groups. The remission and symptomatic group improved on TASIT and RAD from baseline to 24 months. The prodromal progression group improved on TASIT from baseline to 24 months. However, CHR-T did not show improvement on any of the social cognition tasks from baseline to 24 months.

To further explore the characteristics of CHR-T, a GLMM for repeated measures on social cognition was conducted between CHR-T and CHR-NT (Table 2). CHR-T did not differ from the CHR-NT at baseline or at 24 months on the social cognition tasks. CHR-NT showed an effect for time and significantly improved on TASIT, RAD, and ERT (but not EDT) from baseline to 24 months. CHR-T did not show this effect.

#### Discussion

We have previously shown that CHR individuals have lower ToM, emotion perception, and social perception when compared to HC (Barbato et al., 2015; Piskulic et al., 2016). In the current study, we analyzed data from CHR individuals using a comprehensive classification, which separates participants who later have symptomatic remission from those who remain symptomatic and those who transition to psychosis. We found that CHR outcome groups do not differ on social cognition at baseline or 24 months.

Shakeel et al.

In Piskulic et al. (2016), we reported that CHR-T did not differ from CHR-NT on social cognition at 12 month follow-up. In the current study we extended the follow-up period and found that transition to psychosis is not characterized by longitudinal changes in social cognition at 24 months. Additionally, we found that CHR-NT showed an effect for time and improved on social cognition from baseline to 24 months, while CHR-T did not show this effect. Improvements in performance over time observed among CHR-NT is attributable to practice effects which may be task specific (e.g., recall of specific task content) or paradigm specific (e.g., familiarity with task demands, improvements in test taking strategy). However, there is no evidence to suggest that such gains generalize or transfer to other tasks (Goldberg et al., 2010). Poor cognitive functioning in CHR-T, including attention, working memory, and declarative memory deficits (Seidman et al., 2016, 2010; Wood et al., 2007) may account for the absence of practice effects observed among CHR-T in the current study.

We have previously shown that CHR individuals have impairments in social cognition when compared to healthy controls (Barbato et al., 2015; Piskulic et al., 2016). Our current findings show that compared to CHR-NT, CHR-T do not show greater deficits in social cognition at baseline or after transition to psychosis. However, CHR-T fail to show practice related improvements on social cognition over time, so the possibility of further decline as a result of the illness process cannot be precluded.

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#### Table 1.

Generalized Linear mixed model between and within CHR groups for social cognition over time.

	<b>Remission</b> ( <i>n</i> = 109)	Symptomatic $(n = 92)$	Prodromal progression (n = 72)	<b>CHR-T</b> ( <i>n</i> = 86)
Baseline	M (SE)			
TASIT	52.1(0.59)	53.1(0.64)	53.2(0.73)	51.0(0.69)
RAD	31.6(0.50)	32.2(0.54)	32.5(0.61)	31.5(0.59)
ERT	66.9(0.63)	65.7(0.67)	66.0(0.78)	65.0(0.73)
EDT	48.7(1.15)	48.9(1.24)	50.5(1.45)	47.8(1.35)
24 Month	M (SE)			
TASIT	54.9(0.56) <sup>a***</sup>	56.3(0.61) <sup>a***</sup>	55.2(0.69) <sup>a*</sup>	55.5(3.77)
RAD	33.5(0.61) <sup><i>a**</i></sup>	34.8(0.67) <sup><i>a***</i></sup>	33.8(0.75)	36.4(4.31)
ERT	68.8(0.75)	67.8(0.84)	68.5(0.94)	67.7(3.51)
EDT	49.2(1.41)	49.0(1.57)	50.2(1.77)	47.4(6.19)

M= least square mean; SE= standard error of the mean; CHR-T = Clinical High Risk transition to psychosis

\* p<0.05

\*\* p<0.01

\*\*\* p<0.001

 $a^{a}$  = significantly different from baseline

#### Table 2.

Generalized Linear mixed model between CHR-T and CHR-NT for social cognition over time.

	CHR-T ( <i>n</i> =86)	CHR-NT ( <i>n</i> =273)	
Baseline	M (SE)		
TASIT	51.0(0.69)	52.7(0.37)	
RAD	31.5(0.59)	32.1(0.31)	
ERT	65.0(0.74)	66.3(0.39)	
EDT	47.8(1.35)	49.2(0.73)	
24 Month	M (SE)		
TASIT	55.5(3.78)	55.5(0.36) <sup>a***</sup>	
RAD	36.4(4.32)	34.0(0.39) <sup>a***</sup>	
ERT	67.7(3.49)	68.4(0.48) <sup>a***</sup>	
EDT	47.4(6.12)	49.4(0.89)	

M= least square mean; SE= standard error of the mean; CHR-T = Clinical High Risk transition to psychosis; CHR-NT = Clinical High Risk non-transition to psychosis.

\* p<0.05

\*\* p<0.01

\*\*\* p<0.001

 $a^{=}$  significantly different from baseline