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## Age-related trajectories of social cognition in youth at clinical high risk for psychosis: An exploratory study

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Contributors

Dr. Davidson undertook the statistical analyses and wrote the first draft of the manuscript. Drs. Davidson, Johannesen, and Woods contributed to the original conceptualization of the study, and along with Dr. Piskulic wrote subsequent drafts of the manuscript. All of the authors listed were involved in study design and have contributed to and approved the final manuscript.

### Conflict of interest

The Authors have declared that there are no conflicts of interest in relation to the subject of this study. T.D.C. reports that he is a consultant to the Los Angeles County Department of Mental Health and to Boehringer Ingelheim Pharmaceuticals. D.H.M. reports that he is a consultant to Boehringer Ingelheim Pharmaceuticals. S.W.W. reports that during the last 36 months he has received investigator-initiated research funding support from Pfizer and sponsor-initiated research funding support from Auspex and Teva. He has consulted to Merck, Biomedisyn (unpaid), and Boehringer Ingelheim. He has also served as an unpaid consultant to DSM-5. He has been granted US patent no. 8492418 B2 for a method of treating prodromal schizophrenia with glycine agonists and has received royalties from Oxford University Press.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.schres.2018.05.001>.

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## Abstract

**Background:** Clinical high risk (CHR) status is characterized by impairments in social cognition, but questions remain concerning their stability over development. In cross-sectional analysis of a large naturalistic sample, the current study examined whether those at CHR status show deviant trajectories for age-related change in social cognitive ability, and whether these trajectories are influenced by treatment history.

**Method:** Emotion perception (EP) and theory of mind (ToM) were assessed in 675 CHR and 263 healthy comparison (HC) participants aged 12–35. Age effects in CHR were modeled against HC age-expected performance. Prior medication status was tested for interactions with age.

**Results:** CHR exhibited normal age trajectory for EP, but significantly lower slopes for ToM from age 17 onward. This effect was specific to stimuli exhibiting sarcasm and not to detection of lies. When treatment history was included in the model, age-trajectory appeared normal in CHR subjects previously prescribed both antipsychotics and antidepressant medication, although the blunted trajectory still characterized 80% of the sample.

**Discussion:** Cross-sectional analyses suggested that blunting of ToM in CHR develops in adolescence, while EP abilities were diminished evenly across the age range. Exploratory analyses of treatment history suggested that ToM was not affected, however, in CHRs with lifetime histories of both antipsychotic and antidepressant medications. Reduction in age-expected ToM ability may impair the ability of individuals at CHR to meet social developmental challenges in adolescence. Medication effects on social cognition deserve further study.

## Keywords

Theory of mind; Prodrome; Neurodevelopment; Schizophrenia; Pharmacology; Social cognition

## 1. Introduction

Social cognitive abilities develop from early childhood into adulthood (Choudhury et al., 2006; Vetter et al., 2013b). These abilities are needed to attain social skills and function effectively through the major social developmental challenges of adolescence (Aguirre et al., 2008; Gil-Olarte Marquez et al., 2006). Much like basic cognition, social cognition is measured across several domains, including theory of mind (ToM), the ability to use context and awareness of one's own mental processes to make inferences of the intentions of others, and emotion perception (EP), the ability to recognize emotion from more overt facial and vocal cues (Mancuso et al., 2011). Like basic cognition, social cognitive processes and their neural underpinnings appear to mature at different periods of development. For example, one aspect of ToM, perspective taking, matures with age-related improvement in inhibitory control (Burnett et al., 2011; Im-Bolter et al., 2016; Singer, 2006; Symeonidou et al., 2016) and EP abilities are influenced by age of puberty (Blakemore, 2008; Burnett et al., 2011; Grosbras et al., 2007; Scherf et al., 2007; Thomas et al., 2007).

While adolescence typically reflects a period of neural maturation and acquisition of new skills in many areas, mental health problems are also more prominent at this stage. For instance, early indications of compromised social function and stress tolerance are associated with clinical high risk (CHR) of developing psychosis (Addington et al., 2011; Addington and Heinssen, 2012; Ames et al., 2013; DeVylder et al., 2013; Glenthøj et al., 2016; Tarbox and Pogue-Geile, 2008; Thompson et al., 2013). Measured on social cognitive abilities, CHR individuals perform intermediate between those who have developed schizophrenia and their non-affected relatives (Lee et al., 2015), and are impaired across multiple domains in comparison to healthy peers (Lee et al., 2015; van Donkersgoed et al., 2015).

The North American Prodrome Longitudinal Study (NAPLS) consortium recently published data on social cognition in a large cohort of CHR youth in association with symptoms, stability over time, and psychosis conversion (Barbato et al., 2015; Piskulic et al., 2016). The CHR group showed social cognitive deficits at the time of study entry in ToM, facial EP, and social perception that persisted over a two-year follow-up period. Interestingly, these deficits were independent of symptom severity or conversion status. Barbato et al. (2015) also reported significant positive correlations between social cognitive measures and participant age in both CHR and healthy comparison groups. However, this analysis did not determine whether reductions were consistent across age or, instead, pertained to a specific period of development, as suggested by analyses of social and role functioning in this sample (Velthorst et al., 2017).

It remains unclear whether social cognitive impairments in CHR represent different developmental trajectories. Additionally, it is unknown how early pharmacotherapy, commonly used to address attenuated symptoms of psychosis and depression, influences the expression of clinical features presumed to indicate psychosis vulnerability. To address these questions, the current study examined age-related trajectories of social cognition in CHR compared to age-expected ability in healthy comparison (HC) participants. Given evidence for age-related improvement during adolescence (Blakemore, 2008; Burnett et al., 2011; Grosbras et al., 2007; Im-Bolter et al., 2016; Scherf et al., 2007; Singer, 2006; Symeonidou et al., 2016; Thomas et al., 2007) and psychometric stability in psychosis (Davidson et al., 2018; Johannesen et al., 2018; McDonald et al., 2006; Pinkham et al., 2016), this analysis focused on performance-based ToM and EP measures, as opposed to measures of bias or social perception (Buck et al., 2016; Mancuso et al., 2011).

The influence of history of psychotropic medications was also explored to account for differences in individual history with potential impact on brain development (Bangalore et al., 2009; Marshall et al., 2005; Piontkewitz et al., 2011; Teicher et al., 1995). We hypothesized that: 1) age-related trajectories in both CHR and HC would suggest improvement in social cognitive ability from adolescence to young adulthood; 2) age-related trajectories of social cognition will differ between CHR and HC, with lower attainment of age-expected abilities in CHR; 3) age-related trajectories would be lower in CHR participants who converted to psychosis during the study; and 4) following the rationale that duration of untreated attenuated psychotic symptoms influences severity of illness, age-related trajectories in CHR will relate positively to pharmacologic treatment.

## 2. Methods

### 2.1. Participants

Recruitment was conducted under approval of Institutional Review Boards of eight NAPLS consortium sites as part of the NIMH-funded NAPLS 2 study (Addington et al., 2015). A description of participant ascertainment and recruitment procedures is provided elsewhere (Addington et al., 2015). All participants provided written informed consent or assent with parents/guardian consent. Exclusion criteria included: current or lifetime axis I psychotic disorder, current IQ below 70, and past or current history of a clinically significant central nervous system disorder. Additionally, HCs with family history of a first-degree relative with a current or past psychotic disorder were excluded.

### 2.2. Measures

**2.2.1. Diagnosis**—Criteria of Prodromal Syndromes (COPS) were examined using the Structured Interview for Psychosis-risk Syndrome (SIPS) and the Scale of Prodromal Symptoms (SOPS) over four domains (i.e. positive, negative, general, and disorganized) determine CHR status and symptom severity (McGlashan et al., 2010). Methods and results regarding duration of prior prodromal syndrome are provided in Supplement. Criteria for conversion to psychosis are described elsewhere (Addington et al., 2012; McGlashan et al., 2010). Baseline DSM Axis I comorbidity has been previously reported for this sample (Addington et al., 2017).

**2.2.2. Social cognition**—Social cognitive abilities in domains of ToM and facial EP were evaluated using measures validated for psychosis research (Pinkham et al., 2014). The tests used to assess social cognition were selected at the time the NAPLS-II study was planned, and ER40, EDF40, and TASIT were selected for current analysis based on empirical support for their sensitivity to impairment in CHR samples. Briefly, the Social Inference subscale of The Awareness of Social Inference Test (TASIT) (McDonald et al., 2003) assessed ToM; and the Penn Emotion Recognition and Penn Emotion Differentiation tasks (ER40 and EDF40, respectively) (Gur et al., 2002) assessed facial EP.

TASIT is an audiovisual measure with established psychometric properties and ecological validity (McDonald et al., 2006) sensitive to ToM deficits in CHR (Green et al., 2012). The Social Inference subscale consists of 16 short video scenes with contextual cues, where actors are engaged in conversations using lies, conveying a message contrary to what the speaker believes, and conveying sarcasm, where the message is contrary to the actual meaning (s)he means to convey. Following each scene, participants answer questions about what the characters are thinking, doing, feeling and saying. Analyses were based on TASIT Lies and Sarcasm subscales (Mancuso et al., 2011).

ER40 and EDF40, previously validated in CHR (Kohler et al., 2014), comprise colored photos representing facial expressions balanced across gender and race (Caucasian, African-American, Asian, and Hispanic). For ER40, participants identify the emotion expressed in facial stimuli (anger, fear, neutral, happy or sad). For EDF40, participants indicate which of two facial stimuli depict an emotion (happiness or sadness) more intensely.

**2.2.3. Medications**—Details of prescription medication use, including psychotropic medication, were recorded at baseline. Statistical analysis was based on binary (presence/absence) coded history of prior prescriptions and duration (in months) of use as recorded at study entry. Five medication classes were considered: antipsychotic, antidepressant, mood stabilizer, stimulant, and benzodiazepine.

### 2.3. Procedures

Clinical assessments were carried out by experienced research clinicians with excellent inter-rater agreement on prodromal diagnoses ( $\kappa = 0.90$ ) (Addington et al., 2012). Social cognition assessments were conducted by trained raters.

### 2.4. Statistical analyses

Data were collected at a single time point at intake to a larger longitudinal study. Distributional properties of each measure were examined for statistical assumptions and multivariate outliers. Variables with skew  $> \pm 1$  were normalized (skew  $< 1$ ) by square-root or log transform (reflected where necessary). Relationships between age and social cognition were examined first by Pearson correlation, and then by model fitting using the SPSS Curve Estimation function (IBM SPSS Statistics v.23 for Windows). In total, four models were tested, for ER40, EDF40, and TASIT Lies and Sarcasm. The best fitting and most parsimonious terms were entered into multiple regression using SPSS Generalized Linear Models with mean-centered predictors (Hayes, 2015; Motulsky and Christopoulos, 2004). Where social cognitive performance was related to age, differences in slope of this relationship between groups (CHR = 1, HC = 0) were tested as an interaction between age and group. Significant interaction terms were followed up within the CHR sample to test differences in slope between those who converted to psychosis vs. those who did not (converters = 1, nonconverters = 0). All analyses were also estimated controlling for estimated full-scale IQ and estimated premorbid intellectual functioning. Results did not differ unless otherwise indicated.

Transition points along the age dimension at which the CHR vs. HC difference became significant were approximated using the Johnson-Neyman technique in the PROCESS macro (Hayes, 2013, 2015). An informal correlation window technique was employed to observe the strength of age-related curves in different age ranges. Specifically, correlations within expanding age windows (2 to 12 years) were examined to identify the age ranges over which linear relationships across the entire range were strongest. Finally, follow-up analyses explored interactions between candidate explanatory variables (i.e., prior symptom duration, psychotropic medication history) and age-related changes in social cognition in the CHR group, following steps of the previously described interaction analysis. Correlations with symptoms were also calculated to characterize these exploratory subgroups. Variables producing significant interaction terms were then tested for CHR vs. HC differences. Alpha was set at 0.05 for planned analyses due to the relatively low power of interaction terms. Similarly, multiple comparisons were addressed in interpretation rather than mathematically (Rothman, 1990; Saville, 1990), given that our primary hypotheses regarding prodromal status and related characteristics are exploratory, not confirmatory. Specifically, we provide statistical test results for both significant and non-significant comparisons, and we interpret

results tentatively, emphasizing consistency with prior research. Treatment analyses are presented using presence/absence of medication history, and effects were not different when tested based on continuous duration measures.

### 3. Results

#### 3.1. Univariate analyses

Complete baseline social cognitive data were available for 675 CHR and 263 HC participants. Table 1 includes characteristics of the study sample.

ER40 and TASIT were negatively skewed, and appropriately normalized with square-root transformations.

#### 3.2. Age and social cognition relationships

In both groups, all social cognitive variables except for ER40 were positively correlated with age (Barbato et al., 2015), supporting Hypothesis 1. Exponential models were specified given their empirical fit and appropriateness to a developmental growth trajectory:  $Y = \alpha(X)^{\beta}e^{\epsilon}$ , equivalent to  $\ln(Y) = \ln(\alpha) + \beta(\ln X) + \ln(\epsilon)$ , specified as logged-predictor and a log-linked response in SPSS Generalized Linear Models, and logged-predictor and logged-response in PROCESS macro. All analyses were re-estimated with linear and quadratic models and did not differ substantially.

Partially contrary to Hypothesis 2, age-related trajectories of ER40 and EDF40 did not differ significantly between groups (i.e., age \* group interaction term  $p > 0.05$ ). Coefficients for group remained significant; CHR scores were lower on all social cognitive measures (Barbato et al., 2015).

Partially supporting Hypothesis 2, TASIT Sarcasm age trajectories showed a significant group \* age interaction ( $p = 0.011$ ), for which the positive slope of TASIT Sarcasm on age was greater in HC than CHR (Table 2 and Fig. 1). The interaction was not significant for TASIT Lies subscale.

Subsequent analyses found that, across the observed age-range, HC and CHR Sarcasm scores became significantly different at and above age 17.4 years. Correlation windows for the linear relationship between age and TASIT sarcasm showed that, in both groups, correlations were consistently observed only after expanding windows to 4 years. In the CHR group, sarcasm was most positively associated with age in the youngest portion of the sample (approximately 12–17 years old). In the HC group, sarcasm was most highly associated with age between 16 and 21 years. Five-year windows of correlations across samples for both groups are illustrated in Fig. 2.

Within the CHR sample, age-related trajectories of TASIT Sarcasm were not different by conversion status ( $p > 0.05$ ), contrary to Hypothesis 3.



### 3.3. Illness and treatment history

Sixty percent of participants at CHR had a lifetime history of psychotropic medication, consisting primarily of antipsychotics and antidepressants. Initial analyses showed that CHR participants with a history of antipsychotic (AP) or antidepressant (AD) medication had a significantly greater regression slope on age for both TASIT subscales, compared to AP or AD-naïve participants, in partial support of Hypothesis 4.

Analyses of medication combinations revealed that this interaction was driven by participants with a history of *both* AP and AD, not participants with a history of *either* AP or AD, or neither. In other words, participants with a history of AP but not AD, AD but not AP, or neither AP nor AD (altogether, AP&AD-, 79.8% of CHRs) had a lower trajectory of TASIT Sarcasm performance both when compared to HC and when compared to CHR participants with histories of both AP and AD (AP&AD+, 20.2% of CHRs). TASIT Sarcasm age-trajectories for CHR AP&AD+ participants did not differ from HC, and the CHR AP&AD+ age coefficient for TASIT Lies was higher than in HC (Table 2 and Fig. 3).

AP&AD+ participants were 0.71 years younger than AP&AD- ( $t = 1.835$ ,  $p = 0.067$ ), but age did not correlate with duration of AP or AD medication. AP&AD+ participants had more severe negative, disorganization, and general symptoms ( $ps < 0.01$ ) but not positive symptoms ( $p = 0.92$ ) compared to AP&AD-, and greater disorganization symptoms than those with a history of *only* AP or AD ( $ps < 0.01$ ). However, measures of symptom severity did not interact with TASIT age trajectories. Neither TASIT scores nor age predicted conversion status in either medication history group.

IQ and premorbid intellectual functioning estimate were higher in controls than CHR participants (see Barbato et al., 2015) but did not differ by AP&AD status. Age trajectory results did not differ after controlling for either variable.

Duration of prior prodromal syndrome (DPS) results are detailed in a Supplement. Briefly, contrary to Hypothesis 4, trajectories for TASIT Sarcasm did not interact with DPS. Surprisingly, DPS was not associated with age. There was a small relationship with TASIT Lies, such that age and ToM for lies were not related among the 14% of CHR participants with DPS over 1.2 years.

## 4. Discussion

Our main finding is that while both emotion perception (EP) and theory of mind (ToM) increase across ages 12–35 in both HC and CHR, age-related improvement in ToM appears blunted in CHR, particularly for interpretation of more complex social cues involved in sarcasm perception. Trajectories were not different for EP, nor did trajectories of ToM predict conversion to psychosis, contrary to hypotheses. CHR is generally associated with social cognitive deficits (Glenthøj et al., 2016; Piskulic et al., 2016), but on this measure of ToM, the deficit appears to be expressed as a failure to acquire age-appropriate abilities later in adolescence. Notably, deficits in ToM were not evident in the youngest portion of the CHR sample, and only became detectable later in adolescence. This effect could represent a delay in skill acquisition related to neurodevelopment, or reflect secondary consequences of



risk factors for psychosis, including emerging symptoms, impaired stress tolerance, and associated reductions in social opportunity during periods critical to social cognitive development. These results are also consistent with trajectories of social functioning recently described from this sample (Velthorst et al., 2017). On the other hand, sarcasm ToM scores were only different between CHR and HC starting around age 18. It is also possible these results are influenced by a selection bias that we could not detect with available data. For example, it's possible that participants brought to research studies by their parents differ qualitatively from those who are independent. Future research should explicitly collect data to account for such selection biases. These interpretations aside, the primary implication of this finding may be that efforts to find early clinical indicators of psychosis risk must account for ability levels expected of aging adolescents.

Prior research suggests the broad construct of ToM and its neural underpinnings develop through heterogeneous stages across youth (Choudhury et al., 2006; Symeonidou et al., 2016), and further research is required to clarify which tests of ToM are most affected in CHR in relationship to neurocognitive development (Dickinson et al., 2004; Vetter et al., 2013a). Present results based on the TASIT suggest that age interactions could play an important role in CHR research, as might be expected given the broad age range during which prodromal symptoms occur (Gee et al., 2012). It is intuitive that onset of attenuated psychotic symptoms is qualitatively different in grade school than during early adulthood, but clinical assessment approaches used in early detection research have not adopted procedures to reference severity measures to metrics of normal aging. Similarly, major changes in both EP and ToM occur before puberty (Booker and Dunsmore, 2017; Bosco et al., 2014; Choudhury et al., 2006; Flavell, 1999; Im-Bolter et al., 2016; Moran, 2013). The relevance of EP development to CHR may not be ruled out by these results, as the present sample started at age 12. For example, the divergence in age-related EP abilities may occur at a younger age for CHR than we could detect. Our finding of differences in ToM via sarcasm rather than lie detection is likely due to overlapping factors. TASIT Sarcasm items are more psychometrically difficult, and sarcasm perception involves a more skillful and granular application of social inference that is likely to develop later than more blatant inferences used for detecting lies (Im-Bolter et al., 2016; Mancuso et al., 2011; McDonald et al., 2006; Nook et al., 2016; Satpute et al., 2016; Vetter et al., 2013a).

Although the age-window analyses are observational, not truly inferential, the observed correlation between age and sarcasm ToM was highest around the end of high school for control participants (see Fig. 2, 16–21 age block). Correlations were relatively small in CHR participants across age, however, we observe a pattern of change in correlation similar to control participants up until the 16–21 age block, at which point a reduction in correlation strength in CHR opposed the age-related improvement observed in control participants. Combined with the finding that these groups differ in ToM for sarcasm starting at end of high school age, these results suggest CHR participants are less likely to make a developmental increase in advanced ToM abilities at the end of teenage years, which would be entirely consistent with Velthorst et al.'s (2017) observation of developmental changes in social and role functioning. Nonetheless, these interpretations must be interpreted as generated, not confirmed, hypotheses.

Exploratory analyses tested characteristics of CHR participants that might affect age-trajectories of ToM consequent to broader effects on brain development. Analyses of medication history found interactions with ToM trajectories. A large proportion of CHR participants had a history of psychiatric prescriptions, especially antipsychotics (APs) and antidepressants (ADs), consistent with proportions previously reported (Woods et al., 2013). Partially consistent with Hypothesis 4, CHR participants with a history of *both* APs and ADs appeared to have a normal age-trajectory for ToM, similar to healthy comparison subjects, whereas the blunted trajectory that distinguished CHR overall was exhibited by 80% of the sample, those with a history of *either* APs, ADs, or neither. Although CHR participants with a history of both APs and ADs were more symptomatic, symptom severity alone did not account for differences in ToM age-trajectory. Neither APs nor ADs are thought to directly affect social cognition (Sergi et al., 2007). Findings pertaining to medication history could result from additional variables, such as attentiveness of families to early changes in mental health or other unmeasured characteristics for which we have not accounted in this analysis. These analyses are regarded as exploratory in nature and warrant more focused replication with longitudinal data.

It is important to note that significant interactions observed in the present study when age-related trajectories were modeled using exponential terms were also present when trajectories were modeled using linear or quadratic terms. While these results are robust to model choice, nonlinear models may be most suitable for representing trajectories of cognitive development, critical periods, and developmental abnormalities (Thomas et al., 2009).

A notable limitation of the present study is the use of cross sectional rather than longitudinal data to model development. The present data suggest four or more years of longitudinal data would be required to observe within-group change in ToM in relatively small samples, consistent with two-year follow-up reported from this sample (Piskulic et al., 2016). However, applying a developmental framework to cross-sectional data provides an important first step (Thomas et al., 2009). In addition, although the sample size of the current study provides some confidence in generalization, the bulk of the sample was between 15 and 22 years old, and the relatively low representation of 12 and >25 year old participants may limit generalization to the entire 12–35 range. If possible, future research would benefit from a younger sample including pre-pubescence, which may help determine the neurodevelopmental timeline and stability of social cognitive deficits related to psychosis (Barragan et al., 2011; Horton et al., 2017). The relationships between social cognition and age in this study were large ( $\chi^2$  14–46 for sarcasm), but the interaction effects were relatively small ( $\chi^2$  6 to 9 for sarcasm). The number of comparisons were minimized a-priori for primary analyses, but false positives remain possible, and replication is required. Further, while there were no correlations with SOPS positive or negative symptoms in this sample (Barbato et al., 2015), CHR is highly comorbid with nonpsychotic disorders (Rosen et al., 2006), and future work should investigate the role of mood and anxiety symptoms in social cognitive development (Kovacs and Goldston, 1991). Finally, the observed effect of combined antipsychotic and antidepressant medication on age-trajectories was an unexpected and novel finding, and warrants further investigation in prospective study designs.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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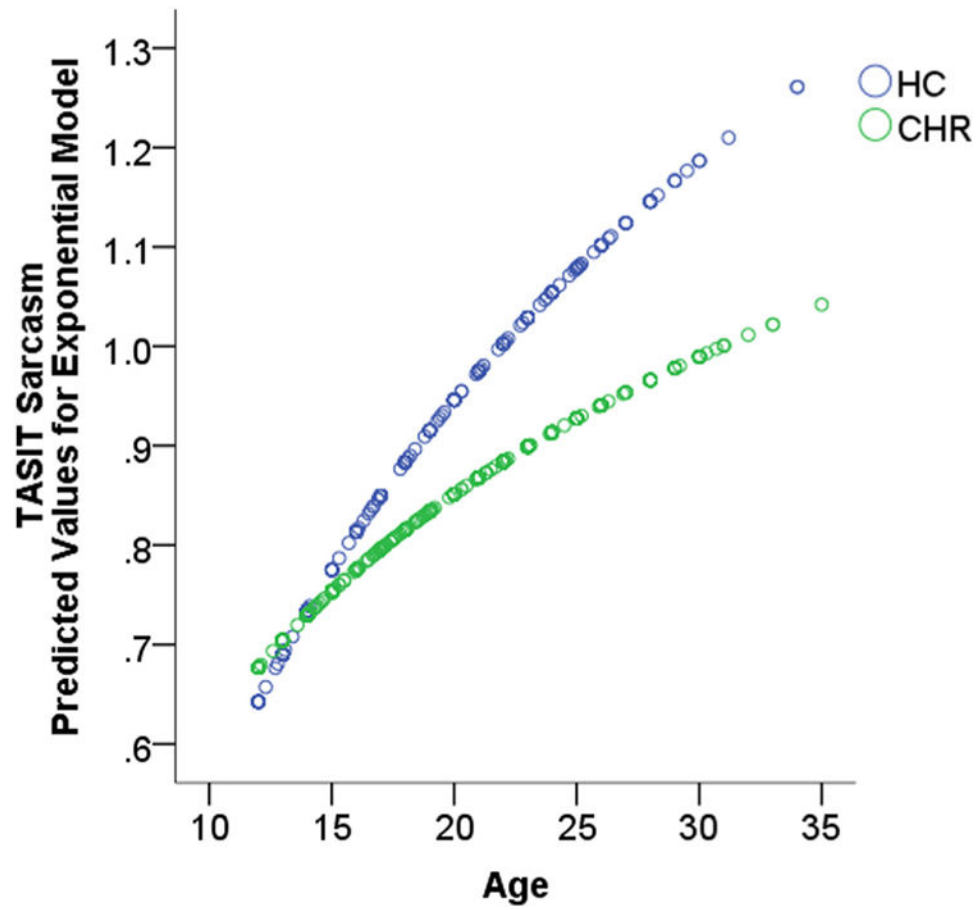
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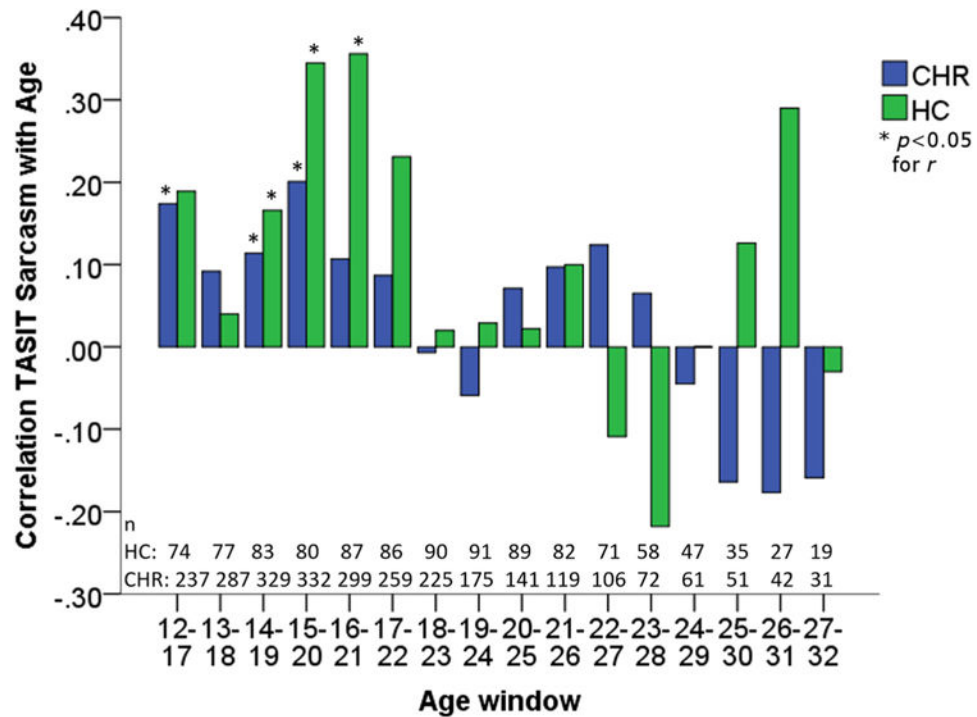
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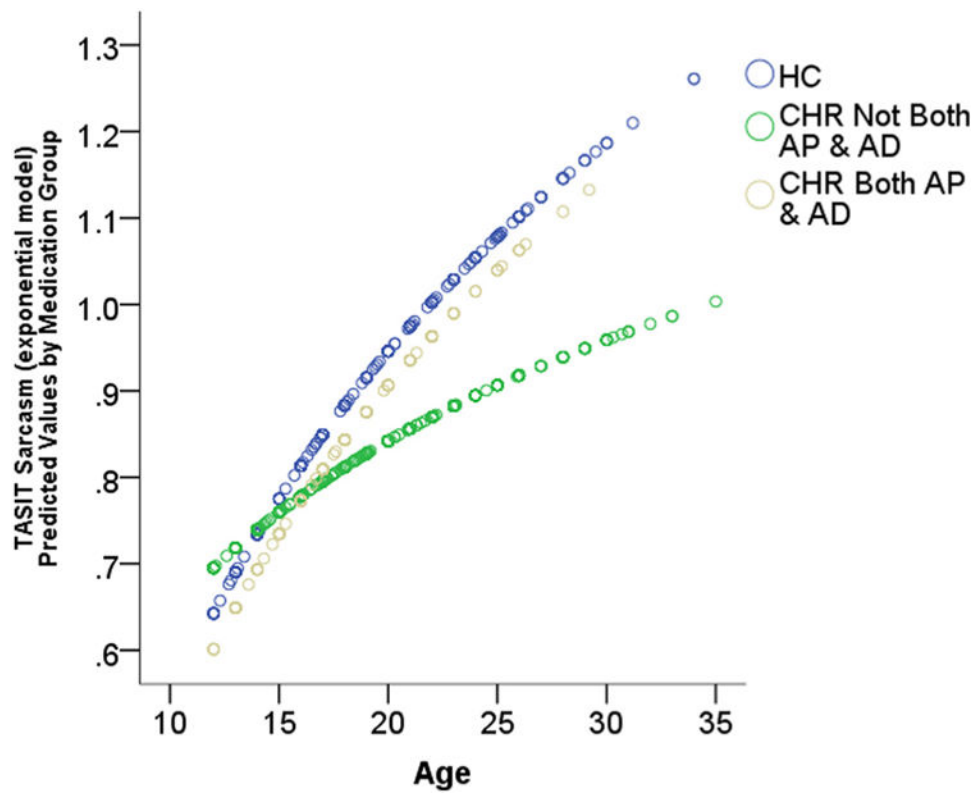


**Fig. 1.** Predicted values for TASIT sarcasm subscale by age. *Note:* HC: Healthy Controls; CHR: Clinical High Risk for Psychosis; TASIT: The Awareness of Social Inference Test, Sarcasm subscale, predicted values for exponential model ( $\ln(X)$  and  $\ln(Y)$ ).





**Fig. 2.** TASIT Sarcasm linear correlations with Age in 5-year windows within CHR and HC. *Note:* n: sample size for age window. HC: Healthy Controls; CHR: Clinical High Risk for Psychosis; TASIT: The Awareness of Social Inference Test, Sarcasm subscale, square-root transformed. \* $p < 0.05$  for correlation ( $r$ ; not a between-groups comparison).



**Fig. 3.** TASIT Sarcasm predicted values (Exponential model) for HC and CHR medication groups. *Note:* HC: Healthy Controls; CHR: Clinical High Risk for Psychosis; AP&AD-: Medication history does not include both antipsychotics and antidepressants; AP&AD+: Medication history includes both antipsychotics and antidepressants; TASIT: The Awareness of Social Inference Test, Sarcasm subscale, predicted values for regression on exponential age model.

Table 1

Demographics of study sample.

	<u>CHR</u> n = 675	<u>Controls</u> n = 263	Test statistic
	Mean (SD)		<i>t</i>
Age in years	18.49 (4.25) <sup>^</sup>	19.80 (4.72) <sup>*</sup>	-4.10 <sup>***</sup>
Years of education	11.28 (2.80)	12.72 (3.59) <sup>**</sup>	-6.53 <sup>***</sup>
	Frequency (%)		$\chi^2$
Sex (% female)	286 (42.4%)	127 (48.3%)	2.69
Race			3.83
First Nations	13 (1.9%)	4 (1.5%)	
Asian	46 (6.8%)	26 (9.9%)	
Black	105 (15.6%)	47 (17.9%)	
Latin American/Middle East/White	425 (63.1%)	157 (59.7%)	
Native Hawaiian/Pacific Islander	3 (0.4%)	1 (0.4%)	
Interracial	82 (12.2%)	28 (10.6%)	
Marital status			0.02
Single never married	642 (95.3%)	250 (95.1%)	
Other <sup>a</sup>	32 (4.7%)	13 (4.9%)	
Currently working	169 (25.1%)	122 (46.4%)	39.96 <sup>***</sup>
Currently enrolled as student	557 (82.8%)	211 (80.2%)	0.83
Medication history			
Any	409 (61.2%)	24 (9.4%)	198.96 <sup>***</sup>
Antipsychotics	188 (28.1%)	3 (1.2%)	81.78 <sup>***</sup>
Antidepressants	293 (43.9%)	12 (4.7%)	127.89 <sup>***</sup>
Antipsychotics & antidepressants	150 (20.2%)	2 (0.7%)	60.84 <sup>***</sup>
Mood stabilizers	57 (8.5%)	1 (0.4%)	20.77 <sup>***</sup>
Stimulants	146 (21.8%)	7 (2.7%)	48.64 <sup>***</sup>
Benzodiazepines	82 (12.3%)	7 (2.7%)	19.24 <sup>***</sup>

<sup>a</sup>Other: Married, divorced, separated, widowed, or cohabiting with a significant other.<sup>^</sup>  
p < 0.10.<sup>\*</sup>  
p < 0.05.<sup>\*\*</sup>  
p < 0.01.<sup>\*\*\*</sup>  
p < 0.001.

**Table 2**

Differences in age-related trajectories of social cognition by group and medication history.

Variable	B <sup>a</sup>	SE (B)	β	χ <sup>2</sup>
TASIT lies				
Age effect by group:				
HC	0.12	0.06	0.09	4.08*
CHR	0.12	0.05	0.09	6.32*
CHR AP&AD-	0.05	0.06	0.04	0.89
CHR AP&AD+	0.49	0.12	0.30	17.89***
CHR converter	0.50	0.47	0.12	1.18
CHR non-converter	0.25	0.14	0.08	3.00 <sup>^</sup>
Group * age interactions				
HC = 0, CHR = 1	0.03	0.10	0.02	0.01
HC = 0, CHR AP&AD- = 1	-0.07	0.08	-0.03	0.62
HC = 0, CHR AP&AD+ = 1	0.38	0.13	0.16	8.97**
CHR AP&AD- = 0, CHR AP&AD+ = 1	0.44	0.13	0.12	10.87**
CHR converter = 0, CHR non-converter = 1	-0.12	0.18	-0.03	0.42
TASIT sarcasm				
Age effect by group:				
HC	0.47	0.07	0.42	46.19***
CHR	0.25	0.05	0.20	24.41***
CHR AP&AD-	0.21	0.06	0.18	13.72***
CHR AP&AD+	0.49	0.12	0.31	16.22***
CHR converter	0.53	0.44	0.14	1.45
CHR non-converter	0.60	0.14	0.19	17.62***
Group * age interactions				
HC = 0, CHR = 1	-0.25	0.11	-0.13	6.54*
HC = 0, CHR AP&AD- = 1	-0.26	0.09	-0.16	8.54**
HC = 0, CHR AP&AD+ = 1	0.01	0.14	0.00	0.01
CHR AP&AD- = 0, CHR AP&AD+ = 1	0.28	0.14	0.08	4.04*
CHR converter = 0, CHR non-converter = 1	0.01	0.18	0.01	0.00

Note: TASIT: The Awareness of Social Inference Test; HC: Healthy Controls; CHR: Clinical High Risk; AP&AD+: CHR participants with a history of both antipsychotic and antidepressant medication; AP&AD-: CHR participants with a history of either or neither, but not both antipsychotic and antidepressant medication.

<sup>a</sup>Parameters are estimated for an exponential model (ln(Y) and ln(X)).

<sup>^</sup>p < 0.10.

\* p < 0.05.

\*\* p < 0.01.

\*\*\*  
p < 0.001.

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