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Demographic correlates of attenuated positive psychotic symptoms

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Abstract

It is now well established that the utilization of standardized clinical criteria can enhance prediction of psychosis. These criteria are primarily concerned with the presence and severity of attenuated positive symptoms. Because these symptom criteria are used to derive algorithms for

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designating clinical high risk (CHR) status and for maximizing prediction of psychosis risk, it is important to know whether the symptom ratings vary as a function of demographic factors that have previously been linked with symptoms in diagnosed psychotic patients. Using a sample of 356 CHR individuals from the NAPLS-II multi-site study, we examined the relation of three sex, age, and educational level, with the severity of attenuated positive symptom scores from the Scale of Prodromal Symptoms (SOPS). Demographic factors accounted for little of the variance in symptom ratings (5–6%). Older CHR individuals manifested more severe suspiciousness, and female CHR participants reported more unusual perceptual experiences than male participants. Contrary to prediction, higher educational level was associated with more severe ratings of unusual thought content, but less severe perceptual abnormalities. Overall, sex, age and education were modestly related to unusual thought content and perceptual abnormalities, only, suggesting minimal implication for designating CHR status and predicting psychosis-risk.

1. Introduction

Extensive research efforts have aimed to understand the causes of schizophrenia and other psychotic disorders, yet the etiological determinants remain largely unknown (Jablensky, 1997). The past decade has been marked by an increased interest in the period of functional decline preceding the clinical onset of psychosis, and this shift in focus has been accompanied by efforts to enhance prospective risk prediction. This period is referred to as the prodrome, and it can last from months to several years (Addington and Heinssen, 2012). Individuals with symptoms characteristic of a prodromal state are often designated as "clinical high risk" (CHR). Characterizing the phenomenology in this period and optimizing clinical prediction of risk for conversion to psychosis are top priorities.

It has been demonstrated that individuals who meet standardized criteria for measuring prodromal signs are at a significantly elevated risk for developing a psychotic disorder within a few years following baseline assessment (Cannon et al., 2008; Nelson et al., 2013; Ruhrmann et al., 2010). In particular, ratings of the severity of attenuated positive psychotic symptoms enhance prediction of subsequent psychosis with noteworthy sensitivity and specificity (Cannon et al., 2008). It is assumed that future refinements of clinical algorithms, as well as the addition of biomarkers, will further enhance prediction and targeted preventive interventions.

It is well-established that demographic factors are associated with both the clinical presentation and progression of psychosis; sex, age, and education level have well-replicated relationships with schizophrenia-spectrum risk rates and symptoms (Choi et al., 2009; Moukas et al., 2010; Willhite et al., 2008). The aim of the current study is to characterize the nature of the relationship between these demographic factors and positive symptoms in CHR individuals to improve prediction of subsequent psychosis, as optimal prediction algorithms may vary as a function of demographic factors. Previous studies of high-risk individuals

suggest that age and sex are not associated with conversion to psychosis (Cannon et al., 2008; Nelson et al., 2013; Schultze-Lutter et al., 2007; Velthorst et al., 2009; Ziermans et al., 2011). Outcomes regarding education, however, are mixed with some finding associations with conversion (Ruhrmann et al., 2010; Schultze-Lutter et al., 2007) and others not (Mason et al., 2004). The current paper aims to explore demographic predictors with specific positive symptoms, the primary determinants of conversion status. If a pattern of symptom presentation can be gleaned, including demographically-related protective factors, there will be significant implications for targeted intervention.

1.1. Sex differences

Research on sex differences across the schizophrenia-spectrum has examined the development, functional impairments, and course of these illnesses. The most well-replicated symptom trends are sex differences in symptom severity; males tend to exhibit greater thought disorder than females (Gur et al., 1996; Thorup et al., 2007a,b), whereas females tend to endorse more auditory hallucinations (Marneros, 1984; Rector and Seeman, 1992; Sharma et al., 1999; Tang et al., 2007; Thorup et al., 2007a,b), paranoia, and persecutory delusions (Andia et al., 1995; Goldstein and Link, 1988; Räsänen et al., 2000; Tang et al., 2007). Although research examining sex differences in CHR samples is limited, the findings to date are consistent with those on schizophrenia; CHR females exhibit greater magical thinking and auditory hypersensitivity (Moukas et al., 2010).

1.2. Age

The modal age range for psychosis onset reflects an earlier age of onset (18–25 years) in males compared to females (25–35 years) (Goldstein et al., 1989; Gureje, 1991; Thorup et al., 2007a,b). Evidence suggests that psychosis onset before age 18 is associated with a more chronic illness course, more severe psychotic symptoms and more severe cognitive impairments (de Girolamo et al., 2012; Mirzakhanian et al., 2013; Walker et al., 2004; Yung et al., 2007). In CHR populations, younger age at onset of CHR syndromes is associated with higher transition rates to psychosis (Yung et al., 2007) and reports of more severe odd beliefs, delusions of reference, unusual perceptions, odd behavior, auditory hallucinations, and physical anhedonia (Bora and Arabaci, 2009; Paino-Pineiro et al., 2008).

1.3. Education

Level of education is most often reported only as a sample characteristic, rather than a variable relevant to illness presentation. Yet, studies of the relation of education with symptom presentation in schizophrenia-spectrum disorders indicate that lower education is associated with more negative symptoms (McGlashan and Fenton, 1992) and poorer prognoses (Wieselgren and Lindstrom, 1996). Studies of those with psychosis have also found that completion of high school (Austin et al., 2013) and generally achieving higher levels of education (Chang et al., 2012; Verma et al., 2012) are predictive of recovery from psychotic illness. Ruhrmann et al. (2010) demonstrated that lower education was a significant predictor of conversion to psychosis in a CHR sample.

1.4. The present study

The North American Prodrome Long itudinal Study (NAPLS) is a multisite study aimed at identifying predictors of the transition to psychosis. NAPLS has a large database of longitudinally followed CHR cases and provides a unique opportunity to examine demographic correlates of symptoms. The present study utilizes the NAPLS-II CHR cohort and focuses on the five SOPS positive prodromal symptoms; unusual thought content, suspiciousness, grandiosity, perceptual abnormalities, and disorganized communication. Our focus is restricted to the positive symptom domain because it is primarily the severity of these symptoms that determines whether individuals are designated as being at CHR for psychosis.

Based on the literature, it is hypothesized that males will demonstrate more disorganized communication, and females will manifest more severe perceptual abnormalities, and suspiciousness. Further, it is hypothesized that younger individuals will exhibit more severe positive symptoms and educational level will be inversely correlated with symptom severity.

2. Method

2.1. Participants

The current sample, recruited for the NAPLS-II study includes 356 CHR individuals. Sample demographic characteristics are presented in Table 1. Participants were excluded from NAPLS-II if at baseline they 1.) met DSM-IV criteria for an Axis I psychotic disorder; 2.) experienced a significant head injury; 3.) met substance dependence criteria within the past 6 months; 4.) had a neurological disorder; or 5.) had a Full Scale IQ <70. More detailed information on the CHR sample is presented in previous reports (Addington and Heinssen, 2012; Addington et al., 2012). Participants were recruited from clinical practitioners as well as newspaper, bus, and online announcements. The current protocol was approved by Institutional Review Boards at all NAPLS sites, and all participants provided informed consent for minors.

2.2. Measures

2.2.1. Prodromal symptomatology—Participants were designated as CHR using the Structured Interview for Prodromal Syndromes (SIPS, Miller et al., 2003). Interview responses were scored by trained interviewers on the Scale of Prodromal Symptoms (SOPS, Miller et al., 2003). The SOPS provides an index of symptom severity that ranges from 0 (absent) to 6 (psychotic) for five symptom domains: unusual thought content, suspiciousness, grandiosity, perceptual abnormalities, and disorganized communication. See Miller et al. (2003) for a detailed description of the five positive symptom categories and SOPS diagnostic criteria for a prodromal syndrome.

2.3. Procedures

At each NAPLS site an initial screening interview was conducted to ensure that the individuals met prodromal criteria on the SOPS. Assessments were conducted by trained interviewers who met reliability standards (Addington et al., 2012). Cross-site reliability in symptom ratings was established before study initiation and on a yearly basis. The kappa

statistic was used to compare interviewer agreement with the gold standard diagnosis on the SOPS ratings. Within all sites, intra-class correlations exceeded .80.

2.4. Data analyses

Correlation and ordinal logistic regression analyses were conducted to explore relationships between demographic variables and SOPS scores. Medication status (on medication versus not on medication) was also included as a predictor in the regression analyses as an index of symptom severity.

3. Results

Pearson and point-biserial (1 = male, 2 = female) correlation coefficients relating the positive symptom scores and demographic variables are presented in Table 2. The severity ratings of all of the symptoms are positively, and in most cases significantly, inter-correlated. Additional correlations for demographic variables and SOPS scores were modest. Female sex and lower educational level were significantly associated with more severe perceptual abnormalities, and older age was associated with greater suspiciousness. Age and education were significantly positively inter-correlated. Sex was unrelated to age or educational level. Independent samples t-tests were conducted for sex and each of the predictor and outcome variables. There were no significant sex differences for age, education, medication status, and SOPS symptoms.

Ordinal logistic regression analyses were conducted separately for each of the five positive symptom indices. In each regression analysis the positive symptom score (P1–P5) was entered as the dependent variable and age, sex, years of education, and medication status (i.e. antidepressants, antipsychotics, stimulants, mood stabilizers) were entered as predictor variables. The models were significant for P1 (unusual thought content), P4 (perceptual abnormalities), and P5 (disorganized communication) symptom domains. See Table 3 for the model and parameter estimates for the SOPS symptoms.

The overall effect of the demographic variables on P1 symptoms accounted for 5% of the variance in symptom severity. Of the predictors only age (Wald χ^2=12.4, $p < 0.001$) and education (Wald χ^2=12.7, $p < 0.001$) were significant. Age was inversely related to P1 symptom severity; younger CHR individuals were more likely to have higher symptom ratings. Conversely, years of education were positively associated with P1 symptom severity; CHR individuals with higher levels of education were more likely to have higher symptom ratings.

The overall effect of the demographic variables on P4 symptoms accounted for 6% of the variance in symptom severity. Sex (Wald $\chi^2 = 7.7$, $p < 0.01$), education (Wald $\chi^2 = 3.4$, $p < .05$), and stimulant medication (Wald $\chi^2 = 4.5$, $p < .05$) were significant predictors. Females were more likely to have higher symptom ratings. Education was inversely related to symptom severity, such that individuals with fewer years of education were more likely to have higher symptom ratings. Finally, CHR individuals who were taking stimulant medication at the time of the assessment were more likely to have higher symptom ratings.

Finally, while the model was not significant for P5, mood stabilizers emerged as a significant predictor. CHR individuals taking mood stabilizers at baseline were more likely to have higher symptom ratings (Wald $\chi^2 = 4.9$, $p < 0.05$).

Ordinal regression analyses were run separately by sex for P4 symptoms to explore the significant sex effect found in the first model. Similar to the main model, symptom ratings were entered as the dependent variable and age, education, and medication status were entered as predictors. The overall effect of demographic variables on P4 was not significant for either females or males. However, for males, education ($\beta = -.19$, Wald $\chi^2 = 5.6$, $p < .05$), was a significant predictor and showed an inverse relationship with symptom severity.

4. Discussion

The present study examined the relationship of demographic factors with positive symptom severity in a CHR sample meeting criteria for a prodromal syndrome. The present analyses revealed that sex, age and education were modestly related to unusual thought content and perceptual abnormalities. While similar findings have been yielded from other studies and research groups (EPOS, Ruhrmann et al., 2010; PACE, Nelson et al., 2013; FETZ, Schultze-Lutter et al., 2007) further exploration is warranted. Some variation in inclusion and exclusion exists across research groups, reflecting somewhat different cohorts. Moreover, previous finding regarding positive symptoms have used a composite score or conversion status; to our knowledge no previous study has examined positive SOPS symptoms, individually.

Age was a significant inverse predictor of unusual thought content. This finding is consistent with previous work showing that younger psychotic patients have more severe symptoms in general (de Girolamo et al., 2012; Mirzakhanian et al., 2013; Walker et al., 2004; Yung et al., 2007). This may be due, in part, to the adverse impact of the disease process on developing cognitive capacities. Also, younger CHR participants may have less ability to reason through and discount unusual ideations.

Sex was significantly associated with perceptual abnormalities; females were more likely to have severe ratings than males. Again, this finding is consistent with past reports that females diagnosed with psychosis manifest more severe auditory hallucinations (Marneros, 1984; Rector and Seeman, 1992; Sharma et al., 1999; Tang et al., 2007; Thorup et al., 2007a,b). However, the proportion of the variance in severity of perceptual abnormalities that was accounted for by sex was very small.

Education yielded a varied pattern of results. While our predictions held for perceptual abnormalities, in that this symptom was more likely to be more severe in those with lower education (Ruhrmann et al., 2010; Wieselgren and Lindstrom, 1996), the opposite was found for unusual thought content. The literature regarding the independent role of education in the presentation of individual positive symptoms is sparse. In general, the available literature suggests that higher levels of education can be protective due to greater cognitive resources and more advanced coping strategies (Austin et al., 2013; Chang et al., 2012; Jonsson and Nyman, 1984; Verma et al., 2012; Wieselgren and Lindstrom, 1996). It has also been

suggested, however, that greater abstract thinking ability may intensify the presentation of some ideational psychotic processes (Chen et al., 1997).

Further exploration of the sex effects found for perceptual abnormalities revealed that males' educational experience characterized the relationship between education and greater likelihood of higher ratings of perceptual abnormalities. Thus, continued educational and academic supports in males may be particularly critical when attenuated symptoms are beginning to develop and/or other risk factors have been identified.

Psychotropic medication was not an exclusion criterion in the present study, yet the proportion of medicated CHR individuals was small (see Woods et al., 2013). Analyses revealed higher ratings individuals taking stimulants at baseline were more likely to report perceptual abnormalities, and individuals taking mood stabilizers at baseline were more likely to endorse and demonstrate higher disorganized scores. Increased SOPS ratings for individuals taking medication is not surprising given that treatment providers are more likely to prescribe psychotropics when symptoms are more severe. Moreover, stimulants have been shown to exacerbate attenuated and clinically significant psychotic symptoms (Sharma et al., 1991). Because these analyses are based on naturalistic data, causal inferences cannot be drawn; medication status can be precipitated by symptom severity and can also affect symptom severity. Nonetheless, the results of these analyses indicate that the effects of medication status on symptom severity are modest.

4.1. Limitations

A limitation of the present study is that sample selection criteria can attenuate the relation between symptom severity ratings and other measures, including demographic factors. CHR individuals are recruited based on the presence of symptoms that fall within predetermined severity windows. As noted, the SOPS utilizes a 6 point scale to rate all symptoms, and designation as CHR requires that the individual manifest a score of 3 to 5 on at least one of the attenuated positive symptoms on the SOPS. At the upper end of the scale, if the individual has a score of 6 (psychosis) on any positive symptom, they are excluded from the sample. As a result, the SOPS, by intention, yields CHR samples that manifest a restricted range of baseline scores on the positive symptom ratings, but not the other symptom domains. Thus, a restricted range of scores will reduce variability and constrain the magnitude of the correlations obtained between the positive symptoms and other measures. The present estimates of the relation between demographic factors and symptom severity hold only for CHR-designated samples.

A second limitation of the current study is that some participants were on psychotropic medication at baseline. Our analyses indicate that the relation of medication with symptom severity ratings is modest, and only reaches significance for stimulants and mood stabilizers. Moreover, excluding those on medication would result in a non-representative sample of CHR individuals (Woods et al., 2013).

4.2. Summary and future directions

While the present study indicates that demographic factors are associated with ratings of some positive symptoms in CHR individuals, overall they account for very little of the

variance. The findings suggest that demographic factors are not influencing prodromal symptom presentation in a manner that would alter detection of CHR syndromes as a function of sex, age, or education. Further, it appears unlikely that these factors will be relevant in the derivation of optimal psychosis-risk prediction algorithms, based on positive symptom ratings at baseline. While similar results have been published from other research groups, replication is important, particularly in light of the variation in inclusion and exclusion criteria across studies that affect the demographic characteristics of the different cohorts (e.g. mean age and education values).

Nonetheless, this remains an empirical question that can be addressed in future studies from the NAPLS project when complete follow-up data are available. At that point, it will be possible to examine potential moderating effects of demographic factors on the prediction of conversion to psychosis based on both clinical symptoms and biomarkers.

Acknowledgments

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Table 1

Demographic and characteristics and baseline SIPS symptom scores for CHR sample.

Variable	CHR (*n* = 356)
Age (mean ± SD)	18.9 ± 4.2
Age range	12–35 years
N < 18 years	155
Sex (*n*, %)	
Male	208 (58.4%)
Female	148 (41.6%)
Years of education (mean ± SD)	
Male	11.6 ± 2.5
Female	11.5 ± 2.9
Total	11.6 ± 2.6
SOPS P1 symptoms (mean ± SD)	3.31 ± 1.4
SOPS P2 symptoms (mean ± SD)	2.93 ± 1.5
SOPS P3 symptoms (mean ± SD)	1.0 ± 1.3
SOPS P4 symptoms (mean ± SD)	2.9 ± 1.5
SOPS P5 symptoms (mean ± SD)	1.8 ± 1.5
SOPS P total (mean ± SD)	12.0 ± 4.1
Medication (*n* on meds, %)	
Antipsychotics	62 (18%)
Antidepressants	94 (28%)
Stimulants	18 (5%)
Mood stabilizers	12 (4%)

Note. P1 = unusual thought content; P2 = suspiciousness; P3 = grandiosity; P4 = perceptual abnormalities; P5 = disorganized communication.

Table 2

Summary of inter-correlations for demographic variables and SIPS positive symptoms in the CHR sample.

Variable	1	2	3	4	5	6	7	8	9
1. Sex	–								
2. Age	−.04	–							
3. Education	−.03	.78**	–						
4. P1: unusual thoughts	−.04	−.07	.04	–					
5. P2: suspiciousness	.05	.12*	.09	.31**	–				
6. P3: grandiosity	−.06	.04	.09	.24**	.12*	–			
7. P4: perceptual abnormalities	.11*	−.10	−.15**	.26**	.09	.02	–		
8. P5: conceptual disorganization	−.08	.00	.06	.22**	.17**	.23**	.02	–	
9. Total positive	.00	.00	.05	.69**	.59**	.54**	.49**	.58**	–

Note. P1 = unusual thought content; P2 = suspiciousness; P3 = grandiosity; P4 = perceptual abnormalities; P5 = disorganized communication.

*
$p < .05$.

**
$p < .01$.

Table 3

Ordinal regression analyses for demographic predictors of positive symptoms.

	Positive symptoms									
	P1		P2		P3		P4		P5	
Predictor	R^2_N	β	R^2_N	β	R^2_N	β	R^2_N	β	R^2_N	β
	.050*		.024		.02		06**		.04	
Age		-.13**		.03		-.02		.02		-.04
Education		.21**		.03		.10		-.12*		11
Sex		.10		-.18		-.10		-.56**		31
BLAP		-.24		-.51		-.10		-.06		.37
BLAD		.33		.10		.16		.13		.09
BLST		.49		-.05		-.23		-.97*		-.41
BLMS		.04		.03		.69		.07		-1.17*
n	356		356		356		356		356	

Note. P1 = unusual thought content; P2 = suspiciousness; P3 = grandiosity; P4 = perceptual abnormalities; P5 = disorganized communication. β = unstandardized coefficient; BLAP = baseline antipsychotic use; BLAD = baseline antidepressant use; BLST = baseline stimulant use; BLMS = baseline mood stabilizer use.

*
p < .05.

**
p < .01.