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Attenuated first-rank symptoms and conversion to psychosis in a clinical high-risk cohort

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Abstract

Aim—We sought to examine attenuated first-rank symptoms (FRS) and subcomponents of the Unusual Thought Content (P.1.) section of the Structured Interview for Psychosis-Risk Syndromes (SIPS) to investigate the robust relationship between total P.1. and conversion. We hypothesized that attenuated FRS would drive the association and, additionally, be most predictive of a schizophrenia diagnosis.

Method—We assessed 189 clinical high-risk participants. Two independent raters separately scored attenuated FRS and each subcomponent of P.1. as if each were the only symptom reported. Total P.1. was also scored. Participants were evaluated for conversion up to 2 years.

Results—While total P.1. score significantly predicted conversion in the 54 converters, attenuated FRS, which were relatively uncommon in this sample, nor any subcomponent of P.1., was independently predictive. FRS did not predict conversion to schizophrenia among 35 subjects.

Conclusion—Although attenuated FRS, and subcomponents of P.1. of the SIPS, did not significantly predict transition to psychosis, our results support previous research affirming the value of total P.1. score as a tool for predicting conversion to psychosis.

Keywords

attenuated psychosis; clinical high risk; conversion to psychosis; first-rank symptoms; positive symptoms

1 | INTRODUCTION

The clinical high-risk state for psychosis (CHR), defined by the presence of sub-threshold positive symptoms, has proven valuable in elucidating the development and progression of schizophrenia and other psychoses (Fusar-Poli et al., 2013). Several semi-structured interviews are used to establish CHR status and conversion to full-blown psychosis, including the Comprehensive Assessment of at Risk Mental States (Yung, Yuen, Phillips,

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Francey, & McGorry, 2003), the Basel Screening Instrument for Psychosis (Riecher-Rössler et al., 2007) and the Structured Interview for Psychosis-Risk Syndromes (SIPS; McGlashan et al., 2013). In the latter, the CHR state is delineated by an Attenuated Positive Symptom Syndrome (APSS), defined by the presence of 1 or more attenuated positive symptoms; specifically, (1) unusual thought content/delusional ideas, (2) suspiciousness/persecutory ideas, (3) grandiosity, (4) perceptual abnormalities/hallucinations and (5) disorganized communication.

Increasing attention has been paid to specific SIPS subscales to identify which best predict transition to psychosis. While the presence of first-rank symptoms (FRS) has a historically predictive relationship for conversion to schizophrenia (Andreasen & Flaum, 1991), only a subset of attenuated FRS are evaluated in a single SIPS scale; namely, P.1. (unusual thought content). P.1. is comprised of 5 subcomponents, including (1) perplexity and delusional mood, (2) first-rank phenomenology, (3) overvalued beliefs, (4) other unusual thoughts/delusional ideas, which includes odd thoughts about the body, one's existence or guilt and (5) non-persecutory ideas of reference (McGlashan et al., 2013). Importantly, recent empirical evidence from the large-scale NAPLS-2 study suggests that total score on P.1. of the SIPS is significantly predictive of transition to psychosis (Addington et al., 2015; Cannon et al., 2016), and has demonstrated external validity in other samples (Carrión et al., 2016; Ruhrmann et al., 2010), including our own (Brucato et al., 2017).

However, as P.1. captures a number of positive symptoms, we sought to clarify which subcomponent drives this relationship. Moreover, we wished to examine the relationship between attenuated FRS (voices conversing, voices commenting, thought echo, somatic hallucinations, thought broadcasting, mind being read, delusional perception, delusion of control or passivity) and conversion. We hypothesized that attenuated FRS would specifically predict an outcome diagnosis of schizophrenia, among those who developed psychosis.

2 | METHOD

2.1 | Subjects

We recruited 189 help-seeking CHR participants through health care providers, clinicians and self-referrals. Following telephone screening, potential participants completed in-person eligibility evaluations. Inclusion criteria were: (1) age 13 to 30 year old; (2) capacity for informed consent or assent; (3) English-speaking and (4) meeting psychosis-risk criteria defined by the SIPS. All participants met for the APSS, defined by the presence of 1 or more attenuated positive symptoms of sufficient severity for at least once per week in the past month. Exclusion criteria included: (1) past or present full-blown psychosis; (2) a nervous system disorder; (3) I.Q. <70; (4) moderate or severe risk of harm to self or others; and/or (5) current substance abuse or dependence. Adults provided written informed consent, while minors provided written assent alongside parental informed consent. This study was approved by the Institutional Review Board of the New York State Psychiatric Institute at Columbia University Medical Center.

2.2 | Clinical assessment

CHR participants were assessed at baseline using version 5.3 the SIPS (McGlashan et al., 2013), a semi-structured interview including 5 positive, 6 negative, 4 disorganized and 4 general symptom subscales, individually rated from 0 to 6 (absent to severe). The attenuated range for positive symptoms includes scores from 3 to 5. Based upon detailed vignettes and rater comments collected via the baseline SIPS, 2 certified SIPS raters independently assigned scores for attenuated FRS, and the 5 subcomponents of P.1. using SIPS scoring methods with above 90% interrater reliability. The details of each vignette are written so that raters can independently assess each symptom category, therefore each rater was given his or her own version of the vignettes, and scored separately. Then, raters met to attain a reliable rating through consensus. Agreed-upon scores of attenuated FRS and P.1. subcomponents were used for analyses. Participants were evaluated approximately every 3 months, for up to 2 years, to determine possible conversion.

2.3 | Statistical analyses

Descriptive statistics, mean differences in baseline demographics and clinical features between converters and non-converters were derived using *t*-tests, Chi-squared tests, and Mann-Whitney *U* tests. Fisher's exact test was used, where warranted by low cell counts. Logistic regression was used to confirm prediction models. Survival analysis was used to predict days to conversion (cox proportional hazards regression). An alpha level of $P < .05$ was considered significant.

3 | RESULTS

The overall CHR sample was young ($M = 20.16$ year, $SD = 3.74$ year), predominantly male (68.7%), and ethnically and racially diverse (30% Hispanic, 20.9% African American and 5.2% Asian American). Of the 36.3% of participants taking medication at baseline, 8.9% were prescribed antipsychotic medication, 14.5% antidepressants and 12.8% were prescribed a combination of both. Converters comprised 28.6% of the sample. Of those that converted, 64.8% received a schizophrenia diagnosis. No demographic differences between converters and non-converters were noted (Table 1).

Attenuated FRS were analysed using *t*-tests, Mann-Whitney *U* tests, and logistic regression to predict conversion. Due to lack of variability in voices conversing, thought echo, thought broadcasting and mind being read, they were excluded from further analyses (less than 3 subjects with a score other than 0). Of those included (voices commenting, somatic hallucinations, delusional perception, delusion of control/passivity), *t*-tests for each individual attenuated FRS showed no differences by conversion status. Logistic regression showed trend-level significance for voices commenting ($\beta = 1.07$, $P = .07$) but non-significant results for the rest; however, results became non-significant when demographic variables were included in the model (all $P > .9$). A Cox proportional hazards regression model censoring non-converters for days to conversion was similarly not significant for this or any other attenuated FRS (all $P > .12$ not including demographic variables and all $P > .13$ including them).

The means and SDs for the 5 subcomponents of P.1. from the SIPS and attenuated FRS are presented in Table 2. The *t*-tests identified no significant differences in P.1. subcomponent scores between converters and non-converters; however, a significant difference in total P.1. score ($P = .003$) was observed, as expected. To further explore whether baseline scores on the P.1. subcomponents predict conversion to psychosis, we performed logistic regression, including scores from the 5 subcomponents in the model. Results indicated that none of the 5 P.1. subcomponents were independently predictive of conversion (Table 2). Results remained non-significant, even when including demographic variables and other SIPS symptoms.

To determine whether baseline first-rank scores differed among converters to schizophrenia vs converters to other psychotic disorders, we performed *t*-tests between the 2 groups. None of the attenuated FRS showed significant effects (all $P > .21$). No significant differences were observed in P.1. first-rank subscore ($P = .19$). Logistic regression showed similar results with models based on attenuated FRS and P.1. subcomponents (all $P > .05$). Results were non-significant after including other SIPS symptoms and demographic variables.

4 | DISCUSSION

In our sample, neither the presence of attenuated FRS nor the 5 subcomponents of P.1. independently predicted transition to psychosis. Although the attenuated FRS, voices commenting, has trend-level significance, this finding would unlikely survive any correction for multiple comparisons given the various tests performed, and that the focus was on delusions, and not hallucinations. We also found that FRS did not predict conversion to schizophrenia among converters, as opposed to conversion to other psychoses. Instead, our results replicated previous findings indicating that P.1. is related to transition to psychosis as a whole (Addington et al., 2015; Cannon et al., 2016), but did not provide evidence to support the claim that attenuated FRS may drive this predictive relationship (note that despite the trend effect observed for voices commenting, this symptom cannot drive the P.1. effect because it is related to perceptual disturbances, and not unusual thought content). A possible explanation could be that since overall severity regardless of specific attenuated delusional ideation is what determines total score on P.1., these symptoms as a whole may contribute to conversion, and may have substantial variability across individuals and symptoms.

A wide variety of symptoms is captured under the umbrella of P.1. on the SIPS. Our attempt to examine attenuated FRS by disentangling singular contributions of P.1. subcomponents on transition to psychosis was novel, in that each subcomponent was individually scored and evaluated to understand the underlying factors which might drive the strong association between total P.1. and transition to psychosis reported in the literature (Addington et al., 2015; Brucato et al., 2017; Cannon et al., 2016; Carrión et al., 2016; Ruhrmann et al., 2010), and replicated herein. Most importantly, this scoring method allows for an examination of a large CHR cohort with attenuated FRS. This provides pertinent information on the link between FRS and full-blown psychosis in that first-rank symptomatology can be attenuated in prodromal populations, which has direct clinical applications. Importantly, FRS can be attenuated if full conviction is not reached, and the individual believes the thoughts are

coming from themselves. This novel scoring method allows for quantifying attenuated FRS in CHR populations, and has important implications for future research. Additionally, by determining scores for each subcomponent of P.1. blind to other subscales of the SIPS, a less biased and more comprehensive evaluation of P.1. subcomponents can be determined with reliable consensus.

Notably, while the sample size is relatively large for a population that is characteristically difficult to recruit, it remains modest for phenomenological research. In addition, the current study was a secondary analysis performed with the goal of generating hypotheses about subcomponents of P.1. of the SIPS, and primarily FRS. While our sample of 189 CHR subjects is one of the largest single-site CHR cohorts available, variability in attenuated FRS was low; therefore, these results will need to be replicated and confirmed in a larger cohort, specifically powered to examine these questions. Future research should focus on identifying more specific patterns of symptoms, ideally strongly associated with biomarkers, to elucidate possible strategies to better predict transition to psychosis so that early intervention programmes can more effectively tailor treatment.

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TABLE 1

Sample characteristics

	Non-converters (<i>n</i> = 135, 71.4%)		Converters (<i>n</i> = 54, 28.6%; schizophrenia diagnosis <i>n</i> = 35, 64.8%)		<i>P</i> value
	<i>n</i> (%)	Mean (SD)	<i>n</i> (%)	Mean (SD)	
Age		20.16 (3.74); <i>n</i> = 134		20.31 (3.91)	<i>P</i> = .80
Gender					$\chi^2 = 3.16$ (df = 2), <i>P</i> = .21
Male	92 (68.7%); <i>n</i> = 134		43 (79.6%)		
Female	41 (30.6%); <i>n</i> = 134		10 (18.5%)		
Transgender	1 (0.7%); <i>n</i> = 134		1 (1.9%)		
Ethnicity					$\chi^2 = 0.13$ (df = 1), <i>P</i> = .72
Hispanic	39 (30.0%); <i>n</i> = 130		17 (31.5%); <i>n</i> = 52		
Race					$\chi^2 = 7.02$ (df = 3), <i>P</i> = .07
White	69 (51.5%); <i>n</i> = 134		17 (31.4%)		
Black	28 (20.9%); <i>n</i> = 134		16 (29.6%)		
Asian	7 (5.2%); <i>n</i> = 134		6 (11.1%)		
More than 1 race	30 (22.4%); <i>n</i> = 134		15 (27.8%)		
Medication					$\chi^2 = 1.57$ (df = 3), <i>P</i> = .67
Antipsychotics	11 (8.5%); <i>n</i> = 129		5 (10.0%); <i>n</i> = 50		
Antidepressants	19 (14.7%); <i>n</i> = 129		7 (14.0%); <i>n</i> = 50		
Both	19 (14.7%); <i>n</i> = 129		4 (8.0%); <i>n</i> = 50		
None	80 (60.2%); <i>n</i> = 133		34 (68.0%); <i>n</i> = 50		
Observation time (months)	20.58 (6.11)				
Days to conversion			275.4 (315.1)		$\beta = 0.65$, <i>P</i> = .12

TABLE 2

Outcomes

	Non-converters (<i>n</i> = 135, 71.4%)		Converters (<i>n</i> = 54, 28.6%; schizophrenia diagnosis <i>n</i> = 35, 64.8%)	
	<i>n</i> (%)	Mean (SD)	<i>n</i> (%)	<i>P</i> value
Total PI score		3.41 (1.05); <i>n</i> = 133	3.93 (1.06)	<i>P</i> = .003
PI subscales (<i>n</i> of subjects scored = 3)				
1. Perplexity and delusional mood (115)		2.67 (1.11)	2.80 (1.17)	β = 0.14, <i>P</i> = .41
2. First rank (76)		1.69 (1.71)	1.80 (1.76)	β = -0.02, <i>P</i> = .83
3. Overvalued beliefs (81)		2.14 (1.11)	2.19 (1.29)	β = 0.07, <i>P</i> = .64
4. Unusual ideas about body, guilt, nihilism, religion (78)		2.03 (1.30)	1.91 (1.29)	β = -0.10, <i>P</i> = .46
5. Non-persecutory ideas of reference (42)		1.31 (1.37)	1.17 (1.33)	β = -0.10, <i>P</i> = .45
Attenuated first-rank (non-converters <i>n</i> = 125, converters <i>n</i> = 46)				
Voices commenting ^a	7 (5.6%)	4.00 (0.00)	7 (15.2%)	4.00 (0.00)
Somatic hallucinations	36 (28.8%)	3.05 (0.23)	15 (32.6%)	<i>P</i> = .75 <i>U</i> = 2806, <i>Z</i> = -0.24, <i>P</i> = .81
Delusional perception	10 (8.0%)	3.50 (0.53)	4 (8.6%)	<i>P</i> = .70 <i>U</i> = 2830, <i>Z</i> = .16, <i>P</i> = .87
Delusion of control or passivity ^a	4 (3.2%)	4.00 (0.00)	3 (6.5%)	4.00 (0.00)

^aSample size was too low to perform a statistical test, so descriptive data are shown.