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Latent class cluster analysis of symptom ratings identifies distinct subgroups within the clinical high risk for psychosis syndrome

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ABSTRACT

The clinical-high-risk for psychosis (CHR-P) syndrome is heterogeneous in terms of clinical presentation and outcomes. Identifying more homogenous subtypes of the syndrome may help clarify its etiology and improve the prediction of psychotic illness. This study applied latent class cluster analysis (LCCA) to symptom ratings from the North American Prodrome Longitudinal Studies 1 and 2 (NAPLS 1 and 2). These analyses produced evidence for three to five subgroups within the CHR-P syndrome. Differences in negative and disorganized symptoms distinguished among the subgroups. Subgroup membership was found to predict conversion to psychosis. The authors contrast the methods employed within this study with previous attempts to identify more homogenous subgroups of CHR-P individuals and discuss how these results could be tested in future samples of CHR-P individuals.

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1. Introduction

Individuals with the clinical high risk for psychosis (CHR-P) syndrome (also known as the psychosis prodrome, schizophrenia prodrome, and ultra-high-risk syndrome) have a 17–25% chance of developing a psychotic illness within two years (Fusar-Poli et al., 2016). However, symptoms and outcomes among CHR-P individuals are highly heterogeneous (Fusar-Poli, 2017). Identifying more homogenous phenotypic subgroups within the CHR-P syndrome may aid in clarifying prognosis, etiology, and response to treatment (Compton et al., 2014).

Valmaggia et al. (2013) applied a latent class cluster analysis (LCCA) to Comprehensive Assessment of At-Risk Mental State (CAARMS) symptom ratings (Yung et al., 2005) of CHR-P participants to identify more homogenous subgroups of CHR-P individuals on the basis of symptom configurations. Their analysis identified four subgroups that varied primarily in terms of symptom severity. Subgroup membership predicted important clinical outcomes, such as rates of conversion to psychotic illness.

In the current study, we apply LCCA to identify subgroups based on symptom ratings from the Structured Interview of Prodromal Symptoms (SIPS) and its companion rating scale, the Scale of Prodromal Symptoms (Miller et al., 2003). Conducting an analysis similar to the one conducted by Valmaggia et al. (2013) has several important functions. Such an analysis can determine whether differences between the SIPS and the CAARMS result in different clustering solutions. While similar, both the SIPS and CAARMS assess content areas not measured by the other. The SIPS and CAARMS also divide up symptomatology differently among their respective symptom rating scales. See Table 1 for a comparison of the symptoms assessed by the CAARMS and SIPS. If a similar cluster structure emerges from the current analysis, this would suggest that the overlapping content of the SIPS and CAARMS is sufficient to identify the same

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Table 1
Comparison of SIPS and CAARMS symptom scales.

Scales with a close counterpart		Scales whose content is divided differently or with only an approximate counterpart		Scales without a clear counterpart	
SIPS	CAARMS	SIPS	CAARMS	SIPS	CAARMS
• Perceptual abnormalities	• Perceptual abnormalities	• Unusual ideas • Suspiciousness	• Unusual thought content	• Impairment in personal hygiene	
• Disorganized speech	• Disorganized speech	• Trouble with focus and attention	• Subjective cognitive changes • Observed cognitive changes	• Bizarre thinking	
• Occupational functioning	• Impaired role function	• Decreased expression of emotion	• Observed blunted affect	• Sleep disturbance	
• Impaired tolerance to normal stress	• Tolerance to normal stress	• Decreased ideational richness	• Alogia		• Aggression
• Avolition	• Avolition/apathy	• Social Anhedonia	• Social isolation		• Subjective bodily sensations
		• Decreased experience of emotion	• Anhedonia • Subjective emotional disturbances • Dissociative symptoms		• Subjective autonomic functioning
		• Motor disturbance	• Observed motor functioning • Subjective motor functioning		• Mood swings
		• Grandiosity	• Mania		
		• Dysphoric mood	• Depression • Suicidality and self-harm • Anxiety • OCD		
		• Odd behavior or appearance	• Disorganized, odd, stigmatizing behavior • Observed inappropriate affect		

Note: No official method exists for linking the SIPS and CAARMS scales. This list of proposed counterparts is subjective and for illustrative purposes.

CHR-P subgroups. Contrastingly, if a different subgroup structure emerges, this would suggest that differences between the SIPS and CAARMS may prevent the identification of one or more of the subgroups identified by the other instrument. A failure of our LCCA to replicate Valmaggia's results might also suggest important differences regarding subject recruitment and other extraneous factors between our sample and Valmaggia's: some authors have cited such recruitment and extraneous factors as a pervasive challenge to developing reliable subtyping strategies generally (Cornblatt et al., 2015).

The goals of this study were: (1) employ LCCA to attempt to identify subtypes/subgroups within the CHR-P syndrome on the basis of symptom ratings and (2) determine if the LCCA-derived subgroups differed in terms of their demographics, clinical symptoms, and rates of conversion to psychotic illness.

2. Methods

2.1. Sample description

Data were collected as part of the first and second iteration of the North American Prodrome Longitudinal Study: NAPLS 1 and NAPLS 2 (Addington et al., 2012, 2007). Detailed information regarding the samples can be found in the referenced papers. Both studies admitted individuals who met criteria for any of three risk syndromes: attenuated positive symptoms (APS), genetic risk and deterioration (GRD), and brief intermittent psychotic symptoms (BIPS). Analyses for this study were restricted to the 356 NAPLS 1 and 737 NAPLS 2 CHR-P subjects who had complete baseline symptom data. One difference between the NAPLS 1 and 2 recruitment criteria was that NAPLS 2 added an additional CHR-P syndrome: being younger than 18-years-old and having a diagnosis of schizotypal personality disorder (YSPD). Nine percent of the NAPLS 2 sample met criteria for YSPD, but only 18 individuals (2.4% of the NAPLS 2 CHR-P sample) met criteria solely for YSPD. The demographics of the NAPLS 1 and 2 samples are shown in Table 2. All procedures were approved by the Institutional Review Board (IRB) at each site. Written informed consent (with assent from participants younger than 18) was obtained from all participants.

2.2. Clinical measures

CHR-P symptoms were assessed using the Structured Interview for Prodromal Syndromes (SIPS) and its companion scale, the Scale of Prodromal Symptoms (Miller et al., 2003). Nineteen SIPS symptom items are rated 0–6 based on their severity and those items are categorized into four domains (positive, negative, disorganized, and general). These domains were modeled after the ones set out by Yung et al. in the CAARMS (Fusar-Poli et al., 2017). Medication history was assessed with a lifetime medication history interview. Individual medications had only been coded into distinct classes and divided between lifetime and current use for the NAPLS 2 dataset, so psychotropic medication history analyses were restricted to the NAPLS 2 dataset. Demographic data were collected using a demographics interview.

2.3. Statistical analysis

Statistical analyses were performed using R version 3.3.1 (R Core Team, 2016) supplemented with the *mclust* package (Fraley et al., 2012; Fraley and Raftery, 2002). The mclust package implements latent class cluster analysis (LCCA) by attempting to identify a best fitting Gaussian finite mixture model—i.e., the one with the lowest Bayesian information criterion (BIC) value—using an expectation-maximization (EM) algorithm. Separate LCCAs were computed for the NAPLS 1 and 2 samples. ANOVA tests, χ^2 tests, and Kaplan-Meir survival analyses were conducted to compare the LCCA-derived subgroups on relevant variables and any significant-tests were followed up with pairwise comparisons. SPSS 17 was used for ANOVA and χ^2 analyses.

3. Results

3.1. NAPLS 1 and 2 sample comparisons

Demographic and SIPS syndrome information for the NAPLS 1 and 2 samples are shown in Table 2. The samples differed significantly in race ($\chi^2 = 50.916$, df = 6, $p < 0.001$): pairwise comparisons are shown in

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