Schizophrenia Research 169 (2015) 169–177

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Severity of thought disorder predicts psychosis in persons at clinical high-risk

Diana O. Perkins [a,*], Clark D. Jeffries [b], Barbara A. Cornblatt [c], Scott W. Woods [d], Jean Addington [e], Carrie E. Bearden [f,g], Kristin S. Cadenhead [h], Tyrone D. Cannon [d,i], Robert Heinssen [j], Daniel H. Mathalon [k], Larry J. Seidman [l,m], Ming T. Tsuang [h], Elaine F. Walker [n,o], Thomas H. McGlashan [d]

[a] Department of Psychiatry, University of North Carolina, Chapel Hill, United States
[b] Renaissance Computing Institute, University of North Carolina, Chapel Hill, NC, United States
[c] Department of Psychiatry, Zucker Hillside Hospital, Long Island, NY, United States
[d] Department of Psychiatry, Yale University, New Haven, CT, United States
[e] Hotchkiss Brain Institute, Department of Psychiatry, University of Calgary, Alberta, Canada
[f] Department of Psychiatry and Biobehavioral Sciences, UCLA, Los Angeles, CA, United States
[g] Department of Psychology, UCLA, Los Angeles, CA, United States
[h] Department of Psychiatry, UCSD, San Diego, CA, United States
[i] Department of Psychology, Yale University, New Haven, CT, United States
[j] National Institute of Mental Health, United States
[k] Department of Psychiatry, UCSF, San Francisco, CA, United States
[l] Department of Psychiatry, Harvard Medical School at Beth Israel Deaconess Medical Center, Boston, MA, United States
[m] Department of Psychiatry, Massachusetts General Hospital, Boston, MA, United States
[n] Department of Psychology, Emory University, Atlanta, GA, United States
[o] Department of Psychiatry, Emory University, Atlanta, GA, United States

ARTICLE INFO

Article history:
Received 31 August 2015
Accepted 6 September 2015
Available online 4 October 2015

Keywords:
Psychosis
High-risk
Risk prediction
Symptom severity
Schizophrenia
Survival

ABSTRACT

Background: Improving predictive accuracy is of paramount importance for early detection and prevention of psychosis. We sought a symptom severity classifier that would improve psychosis risk prediction.
Methods: Subjects were from two cohorts of the North American Prodrome Longitudinal Study. All subjects met Criteria of Psychosis-Risk States. In Cohort-1 (n = 296) we developed a classifier that included those items of the Scale of Psychosis-Risk Symptoms that best distinguished subjects who converted to psychosis from nonconverters, with performance initially validated by randomization tests in Cohort-1. Cohort-2 (n = 592) served as an independent test set.
Results: We derived 2-Item and 4-Item subscales. Both included unusual thought content and suspiciousness; the latter added reduced ideational richness and difficulties with focus/concentration. The Concordance Index (C-Index), a measure of discrimination, was similar for each subscale across cohorts (4-Item subscale Cohort-2: 0.71, 95% CI = [0.64, 0.77], Cohort-1: 0.74, 95% CI = [0.69, 0.80]; 2-Item subscale Cohort-2: 0.68, 95% CI = [0.3, 0.76], Cohort-1: 0.72, 95% CI = [0.66–0.79]). The 4-Item performed better than the 2-Item subscale in 742/1000 random selections of 80% subsets of Cohort-2 subjects (p-value = 1.3E−55). Subscale calibration between cohorts was proportional (higher scores/lower survival), but absolute conversion risk predicted from Cohort-1 was higher than that observed in Cohort-2, reflecting the cohorts' differences in 2-year conversion rates (Cohort-2: 0.16, 95% CI = [0.13, 0.19]; Cohort-1: 0.30, 95% CI = [0.24, 0.36]).
Conclusion: Severity of unusual thought content, suspiciousness, reduced ideational richness, and difficulty with focus/concentration informed psychosis risk prediction. Scales based on these symptoms may have utility in research and, assuming further validation, eventual clinical applications.
© 2015 Elsevier B.V. All rights reserved.

1. Introduction

Development of preventative interventions for schizophrenia requires identifying persons at very high risk. An early study examining psychosis conversion in persons meeting high-risk diagnostic criteria reported a 45% 2-year conversion rate (Yung et al., 2004), however subsequent studies found 2-year conversion rates that ranged from 15 to 30% (Demjaha et al., 2012; DeVylder et al., 2014; Katsura et al., 2014; Lee et al., 2014; Liu et al., 2011; Nelson et al., 2013; Riecher-Rossler et al., 2009; Ruhrmann et al., 2010; Woods et al., 2009; Ziermans et al., 2011). Efforts are needed to improve psychosis risk prediction.

* Corresponding author.
E-mail address: Diana_Perkins@unc.edu (D.O. Perkins).

http://dx.doi.org/10.1016/j.schres.2015.09.008
0920-9964/© 2015 Elsevier B.V. All rights reserved.

Prominent among the scales used to evaluate symptoms associated with psychosis risk is the Scale of Psychosis-Risk Symptoms (SOPS) (McGlashan et al., 2010; Miller et al., 2002). The SOPS comprises 19 symptoms in four domains that include: *positive* (unusual thought content/delusional ideas, suspiciousness/persecutory ideas, grandiose ideas, perceptual abnormalities/hallucinations, disorganized communication), *negative* (social anhedonia, avolition, decreased expression of emotion, decreased experience of emotions and self, reduced ideational richness, reduced occupational functioning), *disorganized* (odd behavior or appearance, bizarre thinking, trouble with focus and attention, impaired hygiene), and *general* (sleep disturbance, dysphoric mood, motor disturbances, impaired stress tolerance). The symptoms evaluated by the SOPS were chosen to reflect broadly the symptoms experienced by persons with schizophrenia during their prodrome.

We sought to identify among items measured by the SOPS subsets that best predicted psychosis conversion. We considered two large independent cohorts, the North American Prodrome Longitudinal Study Cohort-1 and the North American Prodrome Longitudinal Study Cohort-2. This allowed construction of risk prediction subscales in Cohort-1 and evaluation of subscale performance in Cohort-2.

2. Methods

2.1. Subjects

Detailed study methods were reported previously (Addington et al., 2007; Addington et al., 2012; Cannon et al., 2008). In brief, the North American Prodrome Longitudinal Study is a multisite observational study of the predictors and mechanisms of conversion to psychosis in persons meeting Criteria of Psychosis-Risk Syndromes (COPS) (Miller et al., 2003). There were two non-overlapping waves of recruitment, Cohort-1 and Cohort-2. For Cohort-1 a database combined the results *post hoc* from eight independent studies that used a prospective design and similar ascertainment and rating methods (Addington et al., 2007). Cohort-2 was developed as a 2-year prospective collaboration of the same eight sites (Addington et al., 2012). For both cohorts, subjects' ages ranged from 12 to 35. Studies were approved by the sites' Institutional Review Boards, and subjects provided written informed consent or assent, with a parent/guardian consenting for persons under age 18.

Study participants were evaluated using the Structured Interview for Psychosis-Risk Syndromes (SIPS) (McGlashan et al., 2010; Miller et al., 2002) to determine if they met criteria for one or more of the following high-risk syndromes: attenuated psychotic symptoms syndrome; brief intermittent psychotic symptoms syndrome; and genetic risk and deterioration syndrome. The Presence of Psychosis (POP) criteria (McGlashan et al., 2010; Miller et al., 2002) were used to classify a subject as a "converter" to psychosis (see Supplement for detailed criteria). For subjects who converted, date of conversion was estimated by clinical interview and, if available, medical records. *Diagnostic and Statistical Manual IV* (First et al., 2002) (DSM-IV) psychotic disorder diagnosis was based on Structured Clinical Interview for DSM IV (First et al., 2002) performed by trained raters. Subjects were re-assessed every six months by raters. While symptom severity was assessed at baseline, prior to conversion, study raters had access to baseline ratings when evaluating conversion status. There is a possibility that this knowledge could have impacted assessment of conversion. To protect against possible bias all high-risk subjects were reviewed at study entry and at conversion by experts (JA and TM) during a diagnostic conference call, to ensure that criteria were met.

The severity of symptoms was scored on the Scale of Psychosis-risk Symptoms (SOPS) (McGlashan et al., 2010) as follows: 0 = *absent*; 1 = *questionably present*; 2 = *mild*; 3 = *moderate*; 4 = *moderately severe*; 5 = *severe but not psychotic*; and 6 = *severe and psychotic*. To simplify analysis, we rescored mild and questionably present from "1" or "2" to "0". We rescored the threshold severity as follows: "moderate" as "1"; "moderately severe" as "2"; "severe but not psychotic" as "3"; and "severe and psychotic" as "4". Applying our analysis strategy to the original scale had no effect on choice of informative symptoms.

For Cohort-1, raters at each site were trained by the instrument's developers and achieved high inter-rater reliability for high-risk syndrome diagnoses (kappa > 0.80) (Addington et al., 2007; Cannon et al., 2008). In addition several sites participated in an evaluation of symptom scoring reliability, achieving intra-class coefficients of >0.7 for each item (Miller et al., 2003). For Cohort-2, raters were required to have yearly assessments; intraclass correlation coefficients for the SOPS total and positive subscales were required to be >0.8 (Addington et al., 2012).

We excluded from this report subjects who did not meet Criteria of Psychosis-Risk States, who had no follow-up visits, or who had items missing from the baseline SOPS (Fig. 1). The follow-up period for survival analysis was two years (the duration of systematic follow-up for Cohort-2).

2.2. Statistical methods

2.2.1. Classifier development

We sought a "risk prediction subscale" for the SOPS, meaning a sum of chosen items that best identified high-risk subjects who subsequently developed psychosis. We used a simple "greedy algorithm" (Comen et al., 2009; Liu et al., 2005) that first finds the best single item relative to a specified metric. Then, if possible, it finds a second item that, when added to the first, most improves the metric, and so on. The algorithm terminates when no additional items improve the metric. Classifier development implemented the greedy algorithm using five-fold cross validation (Kohavi, 1995) with Excel macros and add-ins (Moons et al., 2012). We excluded a random 25% of the subjects from each group, then randomly partitioned the remaining subjects each into five nearly equal subsets. Four converter and four nonconverter subsets were selected and the algorithm applied to all of the 25 possible combinations of converter and nonconverter subsets. We then randomly re-partitioned the five subsets and repeated the symptom selection process, a total of 20 times, resulting in 500 trials. We then excluded a new random 25% of subjects, and then repeated the entire process 10 times, thus generating 5000 total trials. As each model was built ab initio from subsets of the data, the derived classifiers were not identical. There is a wealth of literature on the merits of various model-building strategies (Hand, 2006; Harrell et al., 1984; Harrell et al., 1996; Kohavi, 1995) but less guidance on strategies to best integrate the multiple derived classifiers. Our approach was to rank the symptoms by their selection frequencies, with the most frequently selected items forming the integrated classifiers.

As part of the classifier development phase (Cohort-1) we used a randomization test (Fisher, 1971 [1935]) to determine whether the derived subscales actually performed better than chance. We did so because modern algorithms are capable of finding patterns even in randomized data due to hidden interrelationships. The area under the curve (AUC) of the receiver operating characteristic (ROC) is a plot of sensitivity (predicted positives/true positives) and 1-specificity (predicted negatives/true negatives), at each possible cut-off point for the scale score. From samples of real data, the typical AUC can be in excess of 0.5, although 0.5 is the expected null value from random classification using prior probability (Rucker et al., 2007). A randomization test requires that pseudo-classifiers are constructed ab initio from pseudo-data with exactly the same algorithm used for true data (Buzkova et al., 2011; Lindgren et al., 1996; Rucker et al., 2007; Smit et al., 2008; Tropsha, 2010). Applying this process 1000 times to Cohort-1 data, we created pseudo-data by randomly assigning subjects to pseudo-groups of "converted" or "nonconverted," preserving original group sizes. Exactly the same classifier construction process as above was applied to the pseudo-data to yield 1000 pseudo-classifiers.

2.2.2. Survival analysis

Validation was done with survival analyses using R version 3.1.2. We used two related measures to evaluate discrimination (Heagerty and

دریافت فوری ← متن کامل مقاله

ISIArticles
مرجع مقالات تخصصی ایران

✓ امکان دانلود نسخه تمام متن مقالات انگلیسی
✓ امکان دانلود نسخه ترجمه شده مقالات
✓ پذیرش سفارش ترجمه تخصصی
✓ امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
✓ امکان دانلود رایگان ۲ صفحه اول هر مقاله
✓ امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
✓ دانلود فوری مقاله پس از پرداخت آنلاین
✓ پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات