The lonely soul wanders: on the role of impaired social functioning in the prediction of a first psychosis

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THE STRAUSS AND CARPENTER PROGNOSTIC SCALE PREDICTS TRANSITION TO PSYCHOSIS IN SUBJECTS CLINICALLY AT HIGH RISK FOR PSYCHOSIS.

ABSTRACT

Objective: To investigate the predictive value of the Strauss and Carpenter Prognostic Scale (SCPS) for transition to a first psychotic episode in subjects clinically at-risk (AR) for psychosis.

Methods: 244 AR subjects participating in the European Prediction of Psychosis Study (EPOS) were assessed with the SCPS, an instrument that has been shown to predict outcome in schizophrenia patients reliably. The follow up period was 18 months.

Results: At 18 months, 37 participants had made the transition to psychosis. SCPS items that remained as independent predictors in the Cox proportional hazard model were: Most usual quality of useful work in the past year (Wald=7.61, p=.006, hazard ratio (HR)=1.49, 95% CI=1.12 / 2.0), Quality of social relations (Wald=7.39, p=.007, HR=1.39, 95% CI=1.10 / 1.77), Presence of thought disorder, delusions, hallucinations, or hallucinations in the past year (Wald=10.33, p=.001, HR=1.88, 95% CI=1.28 / 2.75) and Reported severity of subjective distress in past month (Wald=8.51, p=.004, HR=62, 95% CI=.45 / .86). The SCPS total score was also highly predictive of a first psychotic episode by itself (Wald=18.40, p<.0001, HR=1.10, 95% CI=1.05 / 1.15).

Conclusions: To the best of our knowledge, the present study is the first to reveal that the SCPS has predictive value for transition to psychosis within 18 months in an AR sample, suggesting temporal continuity of predictors of outcome. In combination with other variables, the SCPS could make a valuable contribution to a more accurate prediction of a first psychotic episode in vulnerable populations.
Introduction

Predicting the course of illness in schizophrenia patients has been the topic of numerous papers.\textsuperscript{1-10} Several variables with good predictive validity have been identified repeatedly such as gender, premorbid functioning, age of illness onset, previous psychiatric illness and life stress.\textsuperscript{3,4} One of the most commonly used questionnaires in outcome prediction research is the Strauss and Carpenter Prognostic Scale (SCPS).\textsuperscript{10} Items of this scale have been found to predict outcome at 2, 5 and 11 years follow up.\textsuperscript{7-9}

In these studies, the majority of the patients was diagnosed with schizophrenia and the patients were interviewed at their first admission. At the 11 year follow up, Carpenter and Strauss\textsuperscript{9} investigated intercorrelations between the four dimensions of outcome (i.e. duration of hospitalization in the previous year, frequency of social contact, time spent employed during the past year and symptom severity during the past month). They reported that the concept of loosely linked domains of outcome functioning based on 2 and 5-year follow up observations of this cohort, persist at 11 year follow up, suggesting a temporal continuity in outcome domains that assess functioning and symptoms. Concerning predictors of outcome, patients with more frequent social contacts and more stable heterosexual relationships at initial assessment showed a more favourable outcome with respect to frequency of social contacts. Furthermore, the presence and severity of either thought disorders, delusions or hallucinations at first hospital admission was significantly related to symptom severity at follow up.

For some decades, the focus on prediction of outcome in schizophrenia patients has been extended to prediction of a first psychotic episode.\textsuperscript{11-14} The mainly applied research strategy for revealing possible predictors of a first psychotic episode is following up at-risk (AR) subjects who have been clinically identified by certain criteria that can differ in definition, operationalization and terminology.\textsuperscript{13-16} The transition rates for these AR subjects varies widely (10-56%), which underlines the need to identify signs within this somewhat heterogeneous group that further improve prediction of psychosis.\textsuperscript{17}

Recent attempts have been made to improve the prediction of a first psychotic episode in young people meeting the AR-criteria. In addition to information-processing (e.g. reduction of P300 event-related potential amplitude\textsuperscript{18} and mismatch negativity\textsuperscript{19}) and neurocognitive deficits (e.g. reduced verbal fluency\textsuperscript{20}), it has been shown that among others\textsuperscript{21} a low level of baseline functioning, and in particular social impairments could contribute to differentiating those who eventually do and who do not develop psychosis.\textsuperscript{12, 22, 23} Furthermore, severity of (attenuated) positive symptoms has also been found to be predictive of a first psychotic episode.\textsuperscript{12, 23}

To the best of our knowledge, the value of the SCPS scale in predicting transition to psychosis in subjects at-risk for developing psychosis has not yet been investigated. It is still unclear if a temporal continuity of outcome can already be predicted in the period prior to transition. Unlike other scales used in AR research, the SCPS encompasses all domains of functioning and symptoms relevant for the prediction of outcome in schizophrenia patients. Examining individual SCPS items that demonstrate predictive value for a first psychotic episode may provide insight into factors that play a role in enhanced risk for transition to psychosis and that separate converters form non-converters at baseline.
In addition, better understanding of the predictors of a first psychotic episode may help to identify targets for intervention in individuals AR for psychosis, which in turn may lead to better outcomes.

We hypothesize that SCPS items assessing both positive symptoms and also SCPS items assessing (social) functioning are predictive of a first psychotic episode in AR subjects. Additionally, we hypothesize that the predictors of outcome as assessed with the SCPS in recent onset schizophrenia patients in previous studies are already present in the period prodromal to a first psychotic episode.

Method

2.1. Recruitment

Between August 2002 and April 2006, data were collected from 245 help-seeking individuals (age range 16-35) who met ultra-high-risk and/or ‘cognitive disturbances’ criteria and agreed to participate in the European Prediction of Psychosis Study (EPOS). EPOS is a European collaboration of six centres in four countries: Germany, Finland, The Netherlands and the UK. Referral to the early detection services came from psychiatrists, psychologists, general practitioners, outreach clinics, counselling services or teachers, or was self-initiated.

Inclusion criteria comprised slightly extended ultra-high-risk criteria as assessed with the Structured Interview for Prodromal Syndromes (SIPS 3.0) and cognitive disturbances as assessed by the Bonn Scale for the Assessment of Basic Symptoms – Prediction List (BSABS–P), an abbreviated version of the Schizophrenia Proneness Instrument, Adult version (SPI–A). The ultra-high-risk approach consists of three alternative criteria:

(a) attenuated psychotic symptoms defined by at least one of the following symptoms with SIPS score ‘moderate’ to severe but not psychotic’ (3–5), appearing several times per week for at least 1 week within the past 3 months: unusual thought content/delusional ideas, suspiciousness/persecutory ideas, grandiosity, perceptual abnormalities/hallucinations and/or disorganised communication and, as an extension of the usual SIPS UHR criteria, odd behaviour/appearance;

(b) brief limited intermittent psychotic symptoms (BLIPS) defined by hallucinations, delusions or formal thought disorders occurring within the past 3 months and resolving spontaneously within 1 week scoring ‘severe and psychotic’ (6) on the SIPS and achieving at least a ‘moderate’ score on the respective item of the Positive and Negative Syndrome Scale for Schizophrenia;

(c) genetic risk and functional deterioration defined by a 30% or greater reduction on the Global Assessment of Functioning Scale, modified version (GAF–M) compared with the highest level of previous functioning for at least 1 month within the previous year in combination with a first- or second-degree relative with a history of any DSM–IV psychotic disorder or a DSM–IV schizotypal personality disorder of the index person.
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The ‘cognitive disturbances’ criterion requires the presence of at least two of nine cognitive basic symptoms of at least ‘moderate’ severity (≥3) during the last 3 months and, independent of severity, first occurrence at least 1 year before intake. The nine basic symptoms were: inability to divide attention, thought interference, pressure, and blockage, disturbances of receptive and of expressive speech, disturbance of abstract thinking, unstable ideas of reference, captivation of attention by details of the visual field.

Exclusion criteria were: a low verbal IQ (IQ<85); past or present psychotic episode lasting longer than 1 week (i.e. fulfilling DSM–IV criteria of a brief psychotic episode for at least 7 days, assessed by the Structured Clinical Interview for DSM–IV); and symptoms relevant for inclusion arising from a known general medical disorder or drugs or alcohol dependency. On account of the naturalistic design of the present study, (prior) use of antipsychotics was not considered an exclusion criterion.

The investigation was carried out in accordance with the latest version of the Declaration of Helsinki. The study design was approved by the medical ethics committees of all participating centres. Informed written consent from participants was obtained after the procedure had been fully explained.

2.2. Subject characteristics

Of the total of 245 EPOS participants, 244 participants were interviewed with the SCPS at baseline (137 males, mean age=22.5, SD=5.23). Of these subjects, 35 were lost to follow-up at 9 months and altogether 58 at 18 months. The patient characteristics of the EPOS sample were described previously by Ruhrmann et al. (see this article for an elaborate description of the sample).

At the end of the 18-month follow-up period, 37 participants had made the transition to psychosis. The mean time to transition from baseline examination was 496.8 days (SE= 8.5, 95% CI 480.2–513.6). Diagnoses according to DSM-IV after transition were brief psychotic disorder (n=2 [5.4%], time criterion adapted to BLIPS definition); schizophreniform disorder (n = 3 [8.1%]), schizophrenia (n=23 [62.2%]), schizoaffective disorder (n=3 [8.1%]), and mood disorder with psychotic features (n=6 [16.2%]). Converters group did not differ significantly from non-converters in terms of age, gender and cannabis use.

2.2. Instruments

‘At-risk’ symptomatology

The SIPS 3.0, including GAF–M, was employed to determine the presence, severity and type of the extended ultra-high-risk criteria. The Scale of Prodromal Symptoms (SOPS), the rating scale of the SIPS, has four subscales that include five positive symptom items, six negative symptom items, four disorganisation symptoms items and four general symptom items. All items are rated on a seven-point rating scale anchored from 0 (never, absent) to 6 (severe/extreme – and psychotic for the positive items). Symptomatic criteria for an at-risk state are exclusively based on positive symptom items and, in our extension, the disorganisation symptom odd behaviour/appearance.

The EPOS investigators received extensive training from Dr. Tandy Miller, one of the SIPS authors, including a reliability check after approximately 6 months. The pair-wise interrater concordance of the
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SIPS was 77% and determined acceptable by the training team. The Bonn Scale for the Assessment of Basic Symptoms – Prediction list (BSABS–P)26, 32 was compiled to assess cognitive disturbances. To the item collection of the BSABS–P, three theoretical subscales were defined totalling 33 cognitive, perceptual and motor disturbances assessed on a seven-point severity scale (0–6) with maximum frequency of occurrence during the preceding 3 months as the guiding criterion. The investigators received repeated training by the scale’s first author, Dr. Frauke Schultze-Lutter. Concordance rate with expert rating (F.S.L.) was 87.9%.

2.3. Strauss and Carpenter Prognostic Scale

This scale is composed of 21 items referring to the following variables: quantity and quality of useful work in the past year, social class, social relationships, heterosexual relationships, family history of psychiatric symptoms, action problems (violence and suicidal or homicidal gestures), flat affect, duration of previous hospitalisations, time since first occurrence of psychotic symptoms, ‘presence of thought disorder, delusions or hallucinations in the past year’, ‘presence of depression, hypomania or mania in the past year’, precipitating events, reported severity of subjective distress, ability to meet own basic needs, and usual fullness of life.6-10

Wherever appropriate, the temporal reference for premorbid functioning is the year prior to evaluation. Each item was rated by the interviewer on a 5-point severity scale from 0 (rating indicates a poor prognosis) to 4 (rating indicates a favourable prognosis). For example, item 1B, ‘Most useful quality of useful work in the past year’, considering in regard to person’s age and education would be rated as follows:

4: Very competent
3: Competent
2: Moderately competent
1: Marginally competent
0: Incompetent

Similarly, the 12th item, ‘Presence of thought disorder, delusions or hallucinations in the past year’ is scored:

4: None of any of the above.
3: Minimal presence of any or all of above.
2: Moderate amount or any of above.
1: Relatively severe and/or continuous presence of any or all of above.
0: Severe and/or continuous presence of any or all of above.

Until now, no study has been conducted on the specific psychometric properties of the SCPS in people at-risk for a first psychotic episode. However, the validity of the instrument has been tested in several studies of schizophrenia patients and has shown acceptable internal consistency, test-retest reliability and convergent validity.1
2.4. Follow up

Follow-up assessments with the SIPS and BSABS–P took place at 9 and 18 months. Transition to psychosis was operationalised as a continuation of BLIPS, i.e. any single item on the positive subscale of SIPS (SIPS–Positive) with a score of 6 for more than 7 days.33, 34

Following identification of full-blown psychotic symptoms in the SIPS interview, the diagnostic category on transition was determined by applying DSM–IV criteria30 of psychotic disorders and affective disorders with psychotic features. The time threshold of the Criterion B of ‘brief psychotic disorder’ was adapted to the BLIPS definition. Past and present psychosis as parts of the exclusion criteria as well as psychotic diagnosis on making transition were assessed with the SCID–I.31

2.5. Statistical analysis

Statistical analysis was performed using SPSS (version 18.0) for Windows. Comparisons between the AR group with transition to psychosis (converters) and the AR group without transition to psychosis (non-converters) were made with Pearson’s chi square tests and Mann-Whitney U tests.

Predictors were selected in several steps.35 Firstly, of the 19 potential predictor variables examined, 12 were associated with conversion to psychosis in univariate analyses when changes of the -2 log-likelihood of the model and the Wald statistic became significant (p<0.15). As shown in Table 1, when multivariate analysis was applied to predictors from each assessment domain, which effectively removes redundancy among related measures, the number of predictors meeting the cut-off for inclusion fell to 10. Secondly, we entered retained covariates into a multivariate backward stepwise Cox regression model, p<.05 across domains. To assess the effect of SCPS total score on survival time, a separate Cox proportional hazards analysis was employed.

The center that participants attended was entered as a strata variable in all Cox regressions.36 A survival curve was obtained for SCPS total score using Kaplan Meier survival analysis. For this test, a p value of <.05 was considered statistically significant. SCPS items 2 (Social class) and 11b (What is the longest period that SEVERE psychiatric problems have ever persisted more or less continuously, at least once a week) had > 30% missing values.

Therefore, these items could not be imputed with multiple imputations and these two items were not included in any of the statistical analyses. Social classes as defined by SCPS item 2 (based on the Hollingshead-Redlich publication in 1958)37 were difficult to transpose onto modern European AR subjects. Item 11b showed many missing values due to its non-applicability in a large percentage of the AR subjects who did not have persisting severe psychiatric problems. The other SCPS items had 0.8-3% missing values; these values were imputed with the multiple imputations function of SPSS 18.
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Results

Ten variables were included in the final Cox model (see Table 1). Of these variables, the items that remained in the model as independent predictors were: Most usual quality of useful work in the past year (Beta = -.41, SE = .15, Wald = 7.68, p = .006, hazard ratio (HR) = 1.50, 95% confidence interval (CI) for HR = 1.13 / 2.0), Quality of social relations (Beta = -.33, SE = .12, Wald = 7.39, p = .007, HR = 1.39, 95% CI = 1.10 / 1.77), Presence of thought disorder, delusions, hallucinations, or hallucinations in the past year (Beta = -.63, SE = .20, Wald = 10.33, p = .001, HR = 1.88, 95% CI = 1.28 / 2.75) and Reported severity of subjective distress in past month (Beta = .48, SE = .16, Wald = 8.51, p = .004, HR = .62, 95% CI = .45 / .86). A higher score on this latter SCPS item means more severe subjective distress, indicating a better prognosis as assessed with the SCPS.

Table 1. Potential predictor variables by domain. Bold indicates that the predictor variable met statistical criteria for association with conversion to psychosis

<table>
<thead>
<tr>
<th>Domain</th>
<th>No. of items</th>
<th>SCPS item</th>
</tr>
</thead>
<tbody>
<tr>
<td>Work</td>
<td>2</td>
<td>1A: Quantity of useful work in past year,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1B: Most usual quality of useful work in past year</td>
</tr>
<tr>
<td>Social relations</td>
<td>1</td>
<td>3A: Number of social relations most usual in past year</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3B: Quality of social relationships</td>
</tr>
<tr>
<td>Hetero-sexual relations</td>
<td>1</td>
<td>4: Heterosexual relations most usual in past year</td>
</tr>
<tr>
<td>Treatment</td>
<td>1</td>
<td>5: Treatment facilities used currently</td>
</tr>
<tr>
<td>Family history</td>
<td>1</td>
<td>6: Family history of psychiatric hospitalization</td>
</tr>
<tr>
<td>Onset psychiatric symptoms</td>
<td>1</td>
<td>7: Earliest age of onset of psychiatric symptoms</td>
</tr>
<tr>
<td>Action problems</td>
<td>1</td>
<td>8: Action problems since age 12</td>
</tr>
<tr>
<td>Flattened affect</td>
<td>2</td>
<td>9: Flattened, diminished expression of feeling or emotion in past month</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>1</td>
<td>10: Previous hospitalization (or intense family surveillance)</td>
</tr>
<tr>
<td>Duration of psychiatric symptoms</td>
<td>1</td>
<td>11A: Length of time since first occurrence of hallucinations or delusions,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11C: Longest period that any significant psychiatric symptoms have ever persisted</td>
</tr>
<tr>
<td>Positive symptoms</td>
<td>1</td>
<td>12: Presence of thought disorder, delusions, or hallucinations in past year</td>
</tr>
<tr>
<td>Mood symptoms</td>
<td>1</td>
<td>13: Presence of depression, hypomania, or mania in past year</td>
</tr>
<tr>
<td>Precipitating events</td>
<td>1</td>
<td>14: Precipitating events for most recent psychiatric upset</td>
</tr>
<tr>
<td>Subjective distress</td>
<td></td>
<td>15: Reported severity of subjective distress in past month</td>
</tr>
<tr>
<td>Ability to meet basic needs</td>
<td></td>
<td>16: Most usual ability to meet own basic needs in past year</td>
</tr>
<tr>
<td>Fullness of life</td>
<td></td>
<td>17: Most usual fullness of life in past year</td>
</tr>
</tbody>
</table>

The SCPS total score was also highly predictive of a first psychotic episode by itself (Beta = -.098, SE = .023,
The SCPS total score was also highly predictive of a first psychotic episode by itself (Beta = -.098, SE = .023, Wald = 18.40, p< .0001, HR = 1.10, 95% CI = 1.05 / 1.15). This means that the relative risk of developing a psychosis increased by 10% for every decrease in the SCPS total score of 1.

In the total at-risk group SCPS total scores ranged between 26 and 68 and the mean SCPS score for the UHR group was 48.1 (SD = 7.72, median = 49). When the total group was split according to the mean SCPS total score, the survival distribution differed significantly between the groups with above (n = 117) and below (n= 127) the mean (log rank [Mantel Cox] = 12.86, p < .0001) with those below the mean showing more transitions (Figure 1).

**Figure 1: Survival analysis for 18 month follow up.**
Discussion

To our knowledge, the present study is the first prospective follow-up study examining the utility of the SCPS as a tool for improving prediction of a first psychotic episode. Within this help-seeking population, the SCPS total score contributed to a better prediction of a first psychosis. Individual items that remained in the Cox regression model as independent predictors for conversion to psychosis in our AR group were ‘Most usual quality of useful work in the past year’, ‘Quality of social relations’, ‘Presence of thought disorder, delusions, or hallucinations in the past year’ and ‘Reported severity of subjective distress in the last month’.

The majority of the converters received a diagnosis in the schizophrenia spectrum. In previous research, the SCPS has been used to predict the course of the illness for patients diagnosed with schizophrenia. In contrast, the present study investigates the predictors at an earlier stage, i.e. preceding a first psychotic episode. As expected, the results of the present study indicate a temporal continuity of the predictive value of variables often used in schizophrenia studies, extended to the period before the onset of a first psychotic episode.

Our results with regard to the SCPS item ‘Quality of social relations’, which assesses the number and closeness of social relationships, is in congruence with earlier findings in the same study sample.22 These findings show that the item ‘difficulties in getting along in with people’ of the World Health Organisation - Disability Assessment Schedule-II was a significant predictor for a first psychotic episode. Also in the large independent sample of the North American Prodrome Longitudinal Study (NAPLS), social dysfunction was predictive for a first psychotic episode.23, 38

These findings combined support the hypothesis that the likelihood of transition within an AR group is increased when attenuated positive symptoms are accompanied by social withdrawal. It may be that young people are more prone to make the transition to psychosis when they stop discussing thoughts and experiences with other people, which may reinforce their delusional ideas and paranoia for example.22

Increased severity of subjective distress in the converters compared to the non-converters is also described by Yung et al.39 As opposed to first episode schizophrenia samples,6-10 more severe subjective distress in AR subjects seems to be a negative prognostic factor, i.e. increases the likelihood of transition to psychosis. In AR subjects, increased severity of subjective distress may mirror their relative intact reality testing compared to first episode patients.

Further research could focus on examining whether targeted early interventions directed at the predictive domains may improve outcomes. The reduced work quality may represent the pivotal deficits in schizophrenia and its prodrome in information-processing17,18 (leading to cognitive deficits) and social functioning.22, 23, 38 On the one hand, such deficits may contribute to making it difficult to work. On the other hand, the life structuring effect that is usually provided by work or study may reduce the likelihood of making a transition. At-risk subjects often indicate that they want to work or study, and so encouraging these patients with finding work or schooling tailored to their abilities may help to reduce transition. Individual Placement and Support (IPS) has shown promise for vocational development in patients with a first psychotic episode40 and this approach may also be warranted for at-risk subjects.
Further research is also vital to explore appropriate treatments for positive symptoms in at-risk subjects. Best treatment options for AR positive symptoms are currently unclear. The positive symptoms may be the expression of a underlying biological vulnerability present from early on in life, similarly to fever being a non-specific expression of an underlying illness. Investigating this biological vulnerability, that may incorporate deficits in information-processing, may eventually lead to more accurately targeted treatments of the positive symptoms.

Our results suggest that the SCPS may be useful in AR research. It is valid, is not time-consuming (it can be administered and scored within 10 minutes) and no extensive training is needed to be able to administer this practical and useful scale reliably.

**Limitations**

In spite of the previously described strengths of our study, some critical issues regarding the use of the SCPS in an at-risk sample need to be addressed. Firstly, previous research has shown that outcome in schizophrenia research is not a unitary concept. In the present study, we did approach outcome in at-risk subjects as a unitary concept (transition to psychosis). Future studies should investigate the value of the SCPS in predicting outcomes across diverse domains (i.e. duration of hospitalization in the previous year, frequency of social contact, time spent employed during the past year and symptom severity during the past month). A proportion of non-converters psychosis shows persistently poor social functioning and/or negative symptoms.

Secondly, a methodological issue must be considered. As fitted models always perform in an ‘optimistic manner’ in the model-development data, cross-validation within an independent sample would be useful to control for tailor-made modelling. Although in theory, sample-splitting is an option for model validation in large samples, the limited number of converters in the present study did not allow this for statistical reasons. Existing or future samples of comparable size and risk definition are required to validate our findings.

Thirdly, two items from the SCPS were omitted from the total score due to a large percentage of missing values. The SCPS total score in our study may therefore not be comparable to the SCPS total score reported in other studies investigating schizophrenia patients. In our at-risk group, we only experienced difficulty with two of the 21 items. With this in mind, perhaps the SCPS could be modified slightly to better fit the at-risk patient group.

In conclusion, our study reveals that the SCPS can improve prediction of transition in an already clinically identified at-risk sample in the period before a first psychotic episode. In addition to positive symptoms, quality of work and social relationships as well as subjective distress were independent predictors of psychosis in at-risk subjects. In combination with other variables, the SCPS could make a valuable contribution to a more accurate prediction of a first psychotic episode in vulnerable populations.
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