Emerging symptoms on the pathway to psychosis
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Chapter 7

Factor analysis of the scale of prodromal symptoms: differentiating between negative and depressive symptoms

Rianne M.C. Klaassen, Eva Velthorst, Dorien H. Nieman, Lieuwe de Haan, Hiske E. Becker, Peter M. Dingemans, J. Reinaud van de Fliert, Mark van der Gaag, Don H. Linszen

Factor analysis of the scale of prodromal symptoms: differentiating between negative and depressive symptoms

Visual impression of chapter 7
Abstract:

Background: This study examines the ability of the Scale Of Prodromal Symptoms (SOPS) to differentiate between negative and depressive symptoms in a young help-seeking ultra high risk (UHR) group.

Methods: SOPS-data of 77 help-seeking patients at UHR for psychosis were analyzed with an exploratory factor analysis. The extracted Depression factor was validated with the Beck Depression Inventory (BDI). The extracted SOPS Negative symptoms factor was validated with the Negative symptoms subscale of the Positive and Negative Syndrome Scale (PANSS).

Results: Four factors were extracted from the SOPS: a negative, depression, disorganised and positive factor. The Negative symptom factor consisted of three items: (N1: social anhedonia and withdrawal, N3: decreased expression of emotion; and N4: decreased experience of emotions and self), and could be validated with the PANSS Negative symptoms subscale. The Depression factor was also made up by three items: (G2: dysphoric mood, G4: impaired tolerance to normal stress, and D4: personal hygiene/social attentiveness), and could be validated with the BDI.

Conclusions: Our results suggest that 3 items of the Negative symptoms subscale of the SOPS, 2 items of the General and 1 item of the Disorganisation subscale differentiate validly between negative and pressieve symptoms in an UHR population.
Introduction

The success of early detection and intervention in first episode psychosis of schizophrenia-like disorders has led to an increased interest in the period prior to a first episode of psychosis. (1-3). Commonly, the pre-psychotic phase is denoted as either the Ultra High Risk phase (UHR), or the at risk mental state phase (ARMS). Their criteria can be classified into three categories: attenuated positive symptoms (APS), brief limited intermittent psychotic symptoms (BLIPS) and having a genetic risk combined with reduced social functioning (GRRF). Yung and others found that the psychosis transition risk within a year is 10-40% (4-6). Miller et al. (7) constructed the Structured Interview for Prodromal Symptoms (SIPS) in order to assess the criteria used to identify UHR. Embedded within the SIPS is the Scale of Prodromal Symptoms (SOPS), which is designed to rate the severity of relevant symptoms. The SOPS comprises four factors: positive, negative, disorganized and general symptoms (8). The four symptom domains were constructed on a priori grounds (8) to identify UHR patients. To our knowledge, only one validation study has been performed (9), and this study found three instead of four factors: positive, negative, and a general factor.

Although the inclusion criteria of UHR studies are typically based on the positive domain of the SOPS, authors in both retrospective (10), (11) and prospective cohort studies (5), (12) have highlighted the substantial prevalence of negative (up to 40%) and pressive symptoms (30-40%). The depression and negative symptoms clusters are sometimes difficult to distinguish (6), (9), (12-14). However, several reasons underline the importance of differentiating between these two clusters:

Firstly, differentiation is required for diagnostic purposes in the UHR phase. Negative symptoms, specifically social anhedonia and withdrawal, have been found to predict first psychosis transition in a UHR-group (15-17), whereas pressive symptoms seem to play a minor role as predictor. Young adults suffering from depression can be at risk for psychosis as well as for depression or a bipolar disorder (18).

Secondly, differentiation between negative symptoms and depression may lead to targeted treatment strategies in the UHR phase, specifically when depression is better diagnosed. Treatment strategies for pressive symptoms are well established (for example antidepressant medication or cognitive behavioural therapy (CBT) (19) while specific interventions for negative symptoms are still under development (20), (21). Hawkins et al. (9) concluded that it is possible to differentiate between depression and negative symptoms in an UHR population by means of the SOPS, since the item
We therefore believe that a replication of their factor analysis is needed with specific attention to SOPS negative and depression items. This study focuses on the depression and negative symptom items in an UHR group by performing an exploratory factor analysis of the SOPS. The extracted depression and negative symptoms factors are validated with the golden standard for the Positive And Negative Symptom Scale (PANSS) (22) and with the total score on the Beck Depression Inventory (BDI) (23).

**Methods**

**Subjects**

Help-seeking adolescents were referred by local mental health services to the Early Psychosis Department of the Academic Medical Center (AMC) of the University of Amsterdam, a unit specialized in diagnosis, treatment and research of early psychosis and subjects at UHR for psychosis transition. The inclusion criteria were: ages between 12 and 35 years, being able and willing to give informed consent and falling into one of the following groups:

1: Attenuated Positive Symptom Group (APS): subjects who have experienced one of the following symptoms in a mild to moderate extent: unusual thought content (delusional ideas), suspiciousness (persecutory ideas), grandiosity, perceptual abnormalities (hallucinations), disorganised communications and odd behaviour/appearance.

2: Brief limited intermittent psychotic symptoms (BLIPS): subjects who have experienced episodes of frank psychotic symptoms during the previous year which spontaneously resolved within a week.

3: Genetic risk and reduced functioning (GRRF): subjects who have a first degree relative with a psychotic disorder, or who themselves have a schizotypical personality disorder. Moreover, the subjects had experienced a decrease in functioning, namely a reduction on the Global assessment of Functioning Scale (GAF) (American Psychiatric Association, 1994) of at least 30%, compared to the highest level of their previous functioning for at least one month within the previous year.
The exclusion criteria were: a previous psychotic period for more than one week, a premorbid IQ<85, symptoms due to a known general medical disorder or intoxication with drugs or alcohol. ‘Cannabis use’ in the past or the present was defined as the use of cannabis at least 5 times in a lifetime. Cannabis use was not an exclusion factor in itself, but patients were excluded if they used any other drug or if the cannabis seemed to have caused the UHR symptoms. In order to establish the relation between cannabis use and psychotic symptoms, cannabis-using patients were required to stop taking drugs in the month following intake. Subsequently, they were then assessed again with the SIPS to investigate whether their symptoms remained. If so, they were included in the study.

The investigation was carried out in compliance with the latest version of the Declaration of Helsinki. The study design was approved by the Medical Ethical Committee of the AMC. Informed consent of the participants (and parents if subjects were under 16 years old) was obtained after the nature of the procedures had been fully explained.

**Instruments**

The SIPS was used to assess prodromal symptoms (8). The SOPS was used to rate the severity of symptoms. The SOPS rating scale consists of 19 items (5 positive, 6 negative, 4 disorganisation and 4 general symptoms). Each item is rated on a 7 point scale which covers severity variance in the sub psychotic or attenuated range, varying from 0 (Never, absent) to 6 (Severe/Extreme and Psychotic). Scores of 3 to 5 on the positive items are considered as indicative of the UHR phase (APS). A score of 6 on one of the positive symptom scores means the person is psychotic. All interviewers received a two-day training by Dr. T. J. Miller, key SIPS/SOPS developer and trainer, followed by a reliability check after six months. The pair-wise inter-rater reliability concordance of the SOPS was 77% which was deemed acceptable by the training team. Dysphoric mood is one of the General Symptoms (G2) rated on the SOPS. The score on this item is based on 6 specific questions about mood and mood-related symptoms (i.e. crying, hopelessness, eating problems, sleeping problems, suicidal thoughts, irritability/ aggressiveness and anxiety). The General Assessment Functioning (GAF) of the DSM was used to determine the current and highest level of functioning in the previous year.

The severity of pressieve symptoms was examined with the BDI (23). The BDI is a 21 item self-rating scale. Each item comprises 4 statements that describe symptom severity. It is validated for general and depressed populations (24), (25)
Negative symptoms were assessed with the PANSS (22). It is validated to measure negative symptoms in schizophrenia and related disorders (26). The PANSS is composed of 30 items, (7 negative symptom items) each of which is given an anchored score of 1 to 7. All instruments were administered by trained residents and researchers with extensive clinical experience. The intraclass correlation coefficients for the PANSS positive, negative, and general psychopathology subscales were 0.91, 0.84 and 0.76, respectively.

Procedure

After referral to the AMC, the adolescents and young adults were interviewed by a psychiatrist and psychologist. Parents were interviewed separately about their child’s lifetime history, complaints, family history of psychiatric disorders, substance and medicine (ab)use. The SOPS was rated and each subject was discussed in a case conference. Patients considered to be at UHR were then asked to sign a written informed consent to participate in the Dutch Prediction of Psychosis Study (DUPS). They received an initial assessment after admission into the study in which, amongst other questionnaires, the BDI-I and the PANSS were assessed. The follow-up period was 3 years.

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Science (SPSS), version 16. Differences in symptom severity between the patients using antidepressants and those who did not were examined with two-tailed t-tests. Construct validity of the SOPS was tested by entering the data into a principal component analysis, using Kaiser’s criterion (eigenvalues of 1.0 or more) and scree plot analysis. Varimax rotation was used to rotate, and validation was then carried out by a correlation analysis (Spearman).

As negative symptoms show overlap with pressieve symptoms we wanted to correct for artificial inflation of the size of the correlation coefficient obtained. Partial correlations were therefore used to control for common variance in depression and negative symptoms scales.
Results

Of the 285 referrals to the AMC 108 (37.9%) met the UHR criteria. Of these, 77 adolescents gave written informed consent to take part in the study (table 1).

<table>
<thead>
<tr>
<th>Total referrals</th>
<th>285</th>
</tr>
</thead>
<tbody>
<tr>
<td>No show</td>
<td>17</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Screened with the SIPS</th>
<th>268</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exclusions + reason why excluded from study</td>
<td></td>
</tr>
<tr>
<td>Psychosis</td>
<td>109</td>
</tr>
<tr>
<td>No symptoms</td>
<td>42</td>
</tr>
<tr>
<td>Life time symptoms</td>
<td>4</td>
</tr>
<tr>
<td>Age &lt;12 or &gt;35</td>
<td>2</td>
</tr>
<tr>
<td>Organic illness</td>
<td>2</td>
</tr>
<tr>
<td>Mild intellectual disability</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>UHR</th>
<th>108</th>
</tr>
</thead>
<tbody>
<tr>
<td>No informed consent</td>
<td>31</td>
</tr>
</tbody>
</table>

| UHR cohort | 77 |

Baseline characteristics of the sample

The included group consisted of 77 subjects: the mean age was 19.2 years, (S.D. 3.8) and 51 (66.2%) were men. The mean GAF at intake was 50.1 (S.D. 11.4) and patients on medication were included: the medication prescription at the first diagnostic evaluation was measured by dividing it into four categories: (i) antipsychotic medication: patients using antipsychotic medication and antidepressants, and/or other medication such as benzodiazepines were also assigned to this category, (ii) antidepressants or antidepressants with medication other than antipsychotic medication, (iii) other medication, for instance benzodiazepines, methylphenidate, and/or lithium carbonate, and (iv) no medication. Of the patients, 45 (58.4%) did not use any medication (category iv), 9 (11.7%) patients used an antidepressant (ii), 16 (20.8%) used antipsychotic medication (i); 7 patients (9.1%) fell into category iii. Patients who used antidepressants did not differ from those who did not in terms of negative-, positive- disorganised and depression symptomatology on the SOPS.

Most subjects met the ‘Attenuated positive symptoms criteria’ (n=69), including APS and overlap with one of the other groups. The mean SOPS ratings were 2.20 for positive-,
2.22 for negative-, 2.15 for general- and 1.18 for disorganised symptoms. Items with the highest mean ratings are listed in Table 2.

Table 2 Mean scores per SIPS item (N=77)

<table>
<thead>
<tr>
<th>symptom</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1 Unusual thought content</td>
<td>3.74 ± 1.58</td>
<td>0-6</td>
</tr>
<tr>
<td>P2 Suspiciousness/persecutory ideas</td>
<td>2.56 ± 1.74</td>
<td>0-6</td>
</tr>
<tr>
<td>P3 Grandiose ideas</td>
<td>1.17 ± 1.46</td>
<td>0-5</td>
</tr>
<tr>
<td>P4 Perceptual abnormalities/hallucinations</td>
<td>2.52 ± 1.90</td>
<td>0-5</td>
</tr>
<tr>
<td>P5 Disorganized communication</td>
<td>1.03 ± 1.52</td>
<td>0-6</td>
</tr>
<tr>
<td>N1 Social isolation and withdrawal</td>
<td>2.73 ± 2.00</td>
<td>0-6</td>
</tr>
<tr>
<td>N2 Avolition</td>
<td>2.91 ± 2.00</td>
<td>0-6</td>
</tr>
<tr>
<td>N3 Decreased expression of emotion</td>
<td>1.26 ± 1.46</td>
<td>0-5</td>
</tr>
<tr>
<td>N4 Decreased experience of emotions and self</td>
<td>1.66 ± 1.77</td>
<td>0-5</td>
</tr>
<tr>
<td>N5 Decreased ideational richness</td>
<td>1.18 ± 1.54</td>
<td>0-5</td>
</tr>
<tr>
<td>N6 Deterioration in role functioning</td>
<td>3.57 ± 1.77</td>
<td>0-6</td>
</tr>
<tr>
<td>G1 Sleep disturbance</td>
<td>2.18 ± 1.76</td>
<td>0-6</td>
</tr>
<tr>
<td>G2 Dysphoric mood</td>
<td>3.06 ± 1.51</td>
<td>0-6</td>
</tr>
<tr>
<td>G3 Motor disturbances</td>
<td>0.81 ± 1.43</td>
<td>0-5</td>
</tr>
<tr>
<td>G4 Impaired tolerance to normal stress</td>
<td>2.53 ± 1.98</td>
<td>0-6</td>
</tr>
<tr>
<td>D1 Odd behaviour and appearance</td>
<td>0.44 ± 0.88</td>
<td>0-4</td>
</tr>
<tr>
<td>D2 Bizarre thinking</td>
<td>0.92 ± 1.49</td>
<td>0-6</td>
</tr>
<tr>
<td>D3 Trouble with focus and attention</td>
<td>2.61 ± 1.21</td>
<td>0-6</td>
</tr>
<tr>
<td>D4 Personal hygiene/social attentiveness</td>
<td>0.75 ± 1.23</td>
<td>0-6</td>
</tr>
</tbody>
</table>

Principal component factor analysis of the SOPS

The initial analysis generated 7 components with eigenvalues >1.0. Based upon scree-plot analysis further extractions were limited to four factors, accounting for 46.5 % of the variance. These factors bore a reasonable congruence with the SOPS a priori content areas (table 3).

Of the negative symptom items of the SOPS, three had a single loading on Factor 1. These items were: Social anhedonia and withdrawal (N1), Decreased expression of emotion (N3), and Decreased experience of emotions and self (N4). We denote this as the ‘SOPS Negative symptom factor’.

Factor 2 comprises: Dysphoric mood (G2), Impaired tolerance to normal stress (G4) and Personal hygiene/social attentiveness (D4). We call this the ‘SOPS Depression factor’.

Factor 3 defines the ‘SOPS Disorganisation factor’ with the items: Disorganised communication (P5), Bizarre thinking (D2), Odd behaviour or appearance (D1), and Decreased ideational richness (N5).
The items Unusual thought content/ delusional ideas (P1), Suspiciousness/ persecutory ideas (P2) and Perceptual abnormalities/ hallucinations (P4) loaded on factor 4: ‘the SOPS Positive symptom factor’.

Validation

Table 4 presents the validation of the SOPS sub scale for depression and negative symptoms by means of correlations and partial correlations. The SOPS Depression factor correlates with the BDI total score, while the SOPS Negative factor correlates with the PANSS Negative symptoms total score. The SOPS Negative factor is also associated with the BDI total score. Similarly the SOPS Depression factor correlates with the PANSS Negative symptoms total score.

Depression and negative symptoms have a substantial variance in common. When we partial out the variance from PANSS Negative factor from the association between SOPS Depression factor and the BDI total score, the association still remains significant. The association between both depression scales is not moderated by negative symptoms.
When the common variance with BDI total score is partialled out, the strength of the association between SOPS Negative factor scale and PANSS Negative symptoms total score hardly changes. The association between both negative symptoms scale is not moderated by pressieve symptoms.

**Discussion**

The results of this study suggest that it is possible to differentiate validly between negative symptoms and pressieve symptoms in a group at UHR for a psychosis by means of the SOPS. In particular, ‘social anhedonia and withdrawal’, ‘decreased expression of emotion’ and ‘decreased experience of emotions and self’ appear as specific negative symptoms. On the other hand, ‘dysphoric mood’, ‘impaired tolerance to normal stress’ and ‘personal hygiene/social attentiveness’ can be considered unique pressieve symptoms. However, ‘avolition’ and ‘deterioration in role functioning’ have moderate loadings on both factors, arguing against a strict negative/depressive dichotomy for these items. A possible explanation for this finding is that these two items are part of the described overlap between negative and pressieve symptoms.

Contrary to our expectations, the item ‘dysphoric mood’ loaded secondarily on the positive items cluster. Both UHR and psychosis literature provide possible explanations. Yung et al (5) described the following possible chain of reactions: depression can lead to a negative evaluation of experiences, increasing the level of distress, anxiety

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**Table 4** Spearman’s Rho’s correlation and partial correlation between found SOPS depression factor and negative factor, and BDI total score and the PANSS negative items total score

<table>
<thead>
<tr>
<th></th>
<th>SOPS Depression factor</th>
<th>SOPS Negative factor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BDI</strong></td>
<td>0.59 p&lt;.001</td>
<td>0.44 P&lt;0.001*</td>
</tr>
<tr>
<td><strong>PANSS Negative items</strong></td>
<td>0.34 p=0.04</td>
<td>0.63 p&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>0.36 p=0.02</td>
<td>0.50 p&lt;0.001**</td>
</tr>
</tbody>
</table>

SOPS depressive factor = G2 + G4 + D4
SOPS negative factor  NEG = N1 + N3 + N4
BDI = BDI total sum score
PANSS negative items =N1+N2+N3+N4+N5+N6+N7
*= partial correlation SOPS depression factor and BDI total score corrected for PANSS Negative Items
**=partial correlation SOPS negative factor and PANSS negative factor corrected for BDI total sum score
and depression, which can subsequently cause an exacerbation of positive psychotic symptoms. Another possible explanation can be derived from research with patients with a first psychosis. Drake and colleagues (27) found that paranoid symptoms are strongly correlated with depression.

In addition to the item ‘dysphoric mood’, in our study the item ‘Avolition’, an important negative symptom of schizophrenia (28), (29) showed an unexpected second loading. Besides the loading on the negative factor (in accordance with Hawkins et al. and Miller et al. (9), (8)), we found avolition to load on the depression factor. A possible explanation could be the nuance difference between the absence of intention (negative symptoms), and mood induced inactivity (depression). This subtle difference may become clearer in longitudinal studies, as pressieve symptoms vary more over time than negative symptoms with their trait-like nature (30-32).

The results of this study are in accord with those of Hawkins et al. (9). They also found ‘social anhedonia and withdrawal’, ‘decreased expression of emotion’ and ‘decreased experience of emotions and self’ to load on a negative symptoms factor. This is in concordance with the negative subscale of the SOPS-instrument. Moreover, in accordance with Hawkins et al., the items ‘dysphoric mood’ and ‘impaired tolerance to normal stress’ load together, suggesting that these two items to be specific for depression (especially since they also correlate with the BDI). It should be noted that some items do not consistently load on the same factor. For instance, ‘impairment in personal hygiene and/or social attentiveness’ is a disorganized item in the SOPS and part of the depression factor in our study, whereas the Hawkins’ study suggested it to be part of the negative symptom cluster. The items ‘deterioration in role functioning’ and ‘trouble with focus and attention’ show similar differences in a comparison of the results from the different studies. The problem with construct validity of some items is not unique for the UHR group. The same confusion in psychosis and schizophrenia, led researchers in this field to conclude that double loadings do not automatically point to a diffuse item, but rather point to a complex model of causation of symptoms (33), (34). This complex model of causality might also be applicable to our UHR group. The choice for the BDI as the instrument to rate depression is that it is validated in general populations and in depressed patient groups, and, being a self-report scale, it has good clinical usage. The Calgary Depression Rating Scale (CDS) (35) might be a good candidate for rating depression in the UHR patient group, given the high prevalence of negative symptoms. It is currently investigated in an ongoing early detection and intervention study (EDIE-NL) trial, in the Netherlands.
Finally, we need to point out limitations in our study. We based our results upon a relatively small patient group. Nonetheless, the overlap of our main findings with those reported by Hawkins et al (9) taken in combination with the correlation with standard measurements factor analysis, reinforces the validity of our construct.

In summary, we conclude that the SOPS negative symptoms can be differentiated from pressive symptoms in patients at UHR for psychosis. A confirmatory factor analysis in a larger patient sample to validate the results is needed.

**Acknowledgments**

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**Conflict of interests**

All authors declare that they have no conflicts of interest.
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