PROD-screen – a screen for prodromal symptoms of psychosis

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ABSTRACT *The aim of this study was to describe the PROD-screen, an instrument for screening prodromal symptoms indicating risk for psychotic conversion in the near future. PROD-screen consists of 29 questions assessing performance and symptoms.*

Clinical construct validity was tested by comparing scores from the unselected general population (GP, n = 64) with those of general psychiatric patients from a community mental health centre (CMHC, n = 107). The concordant validity of PROD-screen for prodromal symptoms of psychosis was assessed in a large epidemiologically mixed sample of research subjects (n = 132) by comparing PROD-screen scores with the prodromal diagnosis made by Structured Interview for Prodromal Symptoms as a gold standard.

Using the cut-off point of 2/12 specific symptoms, PROD-screen gave correct classification of prodromal status in 77% of cases, distinguishing prodromal from non-prodromal subjects with reasonable sensitivity (80%) and specificity (75%) in the epidemiologically mixed sample. According to subsample analysis PROD-screen functions well with first-degree relatives of schizophrenic patients and probably also with general population samples, but not with psychiatric outpatients.

In conclusion, PROD-screen is a useful tool for screening prodromal symptoms of psychosis and selecting subjects for more extensive research interviews.

Key words: prodromal symptoms, psychosis, screening

Introduction

In recent years the early detection of psychosis has been a strongly emerging research agenda worldwide (McGlashan, 1996). Most clinical research in this area focuses on prodromal symptoms of psychosis, that is, retrospectively derived descriptions of early symptoms in patients later manifesting psychotic disorders (Yung et al., 1996a), with the intention of finding practicable predictors for later psychosis risk (Salokangas, 2001). The usefulness of these symptom descriptions in a prospective setting is still an open question (Heinimaa et al., 2002). Nevertheless, according to current data, prodromal diagnosis made with a structured interview and using multiple criteria sets defines clinical samples, from which 30% to 50% convert to psychosis during one-year follow up (McGorry, 2001). One of the chief problems hampering prospective research on prodromal stages of psychosis is the low incidence of psychotic disorders; to obtain adequate numbers of cases for follow-up study requires extensive recruitment of research subjects (Häfner, 1992a). Difficulties in recruiting such samples for follow-up studies raise the question whether simple, cheap and rapid screening tools could be developed that focus on detecting prodromal symptoms and that would be helpful in collecting subjects in more extensive research interviews. Ideally this screening would be specific enough to be feasible in general population or different segments of general population but screening focused on a help-seeking clinical population would also be useful for research purposes.

The question has been raised of whether instruments targeting mild or attenuated forms of psychotic

symptoms are able to capture symptoms relevant to psychotic disorders in the first place (Warner, 2001). A recent study by Van Os (Van Os, 2000, 2001) investigated this question empirically. This was a population-based study investigating the prevalence of psychotic symptomatology of different levels of severity as assessed by the Composite Diagnostic Interview (WHO, 1990). According to Van Os's data, there is a strong association between different severity levels of psychotic and psychotic-like symptomatology, speaking for a continuum of psychotic presentations and consequently for the feasibility of screening for pre-psychotic symptoms. The base rate of DSM-III-R non-affective psychosis, on the other hand, was rather low among symptomatic individuals. This speaks for applying the screening procedure to selected populations like clinical outpatients who are already seeking help, rather than to general population samples. Nevertheless, Van Os's data are encouraging in supporting the close association of mild or attenuated forms of psychotic symptoms with true DSM-III-R psychotic states, thus suggesting that symptom-based screening is a real option.

This paper presents an instrument specifically designed to be used for screening for prodromally symptomatic individuals with a high likelihood of fulfilling the diagnosis of prodromal syndrome defined by existing research instruments. The intention is that the instrument could be used both with the general population and the help-seeking clinical population samples collected for research purposes. It is not assumed that the screen would be readily applicable to ordinary clinical work as the relevance of the prodrome concept for practical, prospectively oriented clinical work remains unclear.

Prediction of psychotic conversion

Existing data on the validity of prospective prediction of psychosis risk stems from studies by the Melbournian and the Yale group. McGorry's Melbournian group has consistently applied the strategy (Yung, 1996a) of concentrating their sampling efforts to epidemiologically high-risk groups (high familial risk, young help-seeking populations). The prodromal diagnosis is made according to CAARMS criteria (Yung, 1996b; Yung, 1996c). Existing data speak for the strength of this strategy. In the largest of their studies they followed 49 subjects identified with CAARMS criteria up to 12 months and found that 41% had converted to psychosis (Thompson, 2001).

The Criteria of Prodromal States (COPS) criteria used by McGlashans's group in New Haven, Connecticut (Miller, 1999) present only minor modifications to the Australian criteria. The prodromal diagnosis made by the SIPS interview (Structured Interview for Prodromal Symptoms) and applying COPS criteria has good predictive validity. In their longitudinal study prodromal patients converted to schizophrenic psychosis at a 46% rate by six months and at a 54% rate by 12 months (Miller, 2002).

As for case recruitment, McGorry and his group (Yung, 1996c) relied on an extensive network of contacts with various human service providers, public visibility of the early psychosis agenda, and telephone screening to enable case detection. Selection for diagnostic investigation took place in a telephone interview where experienced clinicians assessed likelihood of risk state. In their published data (Yung, 1996c) 86% of presented cases were invited for further evaluation and, although almost a quarter of this group failed to attend, of those who remained 73% were prodromal according to CAARMS criteria (55% of all referrals invited for further evaluation), implying a rather high yield for their telephone-screening procedure. The fact that more than half of the referrals came from a local first episode psychosis unit probably explains the high base rate of true prodromals in this referral sample. Unfortunately, explicit descriptions of case selection by this telephone-screening procedure are not available and neither are there data about frequency of false negative cases.

Likewise, in McGlashan's study, case recruitment has mostly relied on educational work with healthcare networks and personnel, social workers, and relatives' organizations. Initial evaluations by telephone collect basic information about the case and the presenting problem. The majority of referrals come from healthcare professionals and approximately 40% of telephone contacts have led to further diagnostic evaluation. No explicit criteria for case selection are available from this study group.

The data form Melbourne and Yale together with Van Os's epidemiological data speak to the feasibility of collecting prodromal cases from *recently ill* clinical populations, such as new admissions to open care units like mental health centres or policlinics. Creating a sensitive and reasonably specific instrument for screening these populations could be of great value in

systematic evaluation of these clinical populations and for selecting cases for more comprehensive and time-consuming research interviews.

On the basis of these considerations we initiated the DEEP-project (DEtection of Early Psychosis). This is a prospective follow-along study of risk symptoms for psychotic conversion in several clinical and non-clinical samples (Salokangas, 2001). For this study we developed the PROD-screen, a screening instrument for prodromal symptoms of psychosis. In this paper the development and the structure of this instrument are described and its functioning in different samples of non-patient and patient populations is evaluated.

Existing screening instruments

At the moment there are no published instruments specifically meant for screening prodromal cases. The DSM-III-R list of prodromal symptoms has nevertheless been used for screening purposes. This list of symptoms prevalent in pre- and post-psychotic stages of schizophrenia was originally included in the DSM-III due to the requirements of the duration criterion (Spitzer, 1978). The results of subsequent studies showed that this was not suitable for screening purposes. First, in Falloon's Buckingham County study (Falloon, 1992), general practitioners screened primary care populations with a DSM-III-R list of prodromal symptoms. Only 2.5% of subjects screening positive according to the DSM-III-R list turned out to be truly prodromal (Falloon, 1992). Second, in an Australian school survey study the DSM-III-R list of prodromal symptoms was used as a self-administered questionnaire among non-clinical adolescent populations (McGorry, 1995). Among 16-year-old teenagers, up to 50% would be prodromal syndrome positive if the DSM-III-R prodromal symptoms were the criteria – a finding clearly inconsistent with the expected base rate of prodromal psychosis in this age group.

Horneland et al. (2002) recently published a study investigating the prevalence of DSM-III-R 'prodromal' symptoms amongst non-psychotic outpatients and their predictive power for psychosis in a six-month follow up. It was found that these symptoms are common among non-psychotic outpatients, and that most of them do not predict psychotic conversion. Nevertheless, three symptom descriptions (persistent peculiar behaviour, magical thinking and unusual perceptual experience), which had a very low prevalence, were indicative of future psychotic conversion (3/20 subjects with one of more of these symptoms became psychotic in six months). These results speak for the potential of finding valid symptomatic predictors but also show that DSM-III-R list of prodromal symptoms as a whole is a poor instrument for this purpose.

Development of the instrument

The following issues were given special consideration in developing the instrument:

- it should be amenable for both telephone interviewing and self-rating;
- the acceptable length of the interview should not exceed 30 minutes to enhance compliance and save resources;
- the issue of sensitivity should take precedence over specificity as minimizing the rate of false negative cases is considered a priority in screening;
- the screen should be both user and client friendly, easily understandable and use a non-pathologizing style of inquiring of about possible symptoms for ethical reasons (Heinimaa, 1999) and to enhance willingness to complete the interview;
- the indicators of the prodromal state should cover what is currently known about prodromal symptomatology but the instrument should also be able to recognize uncharacteristic forms of subjective experience, symptom formation and behavioural change potentially relevant to incipient psychotic state (Kim, 1994; Parnas 1999).

Contents of the instrument

The development of the screen started with a review of current literature on prodromal symptoms of schizophrenic or other psychoses (Häfner, 1992a; Gross, 1992; Klosterkötter, 1997; Yung, 1996a). The role of mild forms of psychotic symptoms (so- called basic symptoms) or attenuated psychotic symptoms (Yung, 1996a), was assessed in the literature in various ways. The German group emphasizes the specificity of cognitive and information processing deviances for later psychotic episodes (Klosterkötter, 1997). The Australian group, on the other hand, points out that, beside psychotic-like symptoms, prodromal patients manifest abundant affective and general symptomatology and in addition they emphasize that the significance of decline in social and general functioning is a common early manifestation of impending psychosis (Yung, 1996a).

In developing the screen the greatest emphasis was given to symptoms that resemble mild forms of psychotic symptoms such as delusional, hallucinatory, or cognitive disturbances. Twelve different symptom descriptions were described, and this group of *specific* symptoms forms the core of the symptom section in PROD-screen. In their actual formulation, these symptom descriptions were specifically informed by the formulations of relevant symptoms included in the IRAOS (Interview for the Retrospective Assessment of the Onset of Schizophrenia – Häfner, 1992b), BSABS (Bonn Scale for the Assessment of Basic Symptoms – Gross, 1987) and SIPS (Structured Interview for Prodomal Symptoms) (McGlashan, 1998). In addition, nine questions inquiring about general and affective symptomatology were included. To ensure adequate coverage of relevant symptomatology, the following criteria for symptom inclusion were used:

- all main symptom categories (positive, negative, disorganised and general) evaluated in the SIPS (Structured Interview for Prodromal Symptoms) were covered;
- all general and specific symptom categories reported by McGorry as typical in prodromal period were covered (Yung, 1996a);
- all symptom descriptions defined by the IRAOS and with prodromal prevalence higher that 50% in early stages of broadly defined schizophrenic psychosis according to Häfner's ABC-study were covered (Hambrecht, 1994);
- eight basic symptoms defined by BSABS and with the highest discriminating value in predicting future schizophrenic psychosis in the Bonn-Aachen prospective early recognition study of schizophrenia (Klosterkötter, 1997) were covered.

The 21-symptom criteria of the PROD-screen, along with the specific sources (SIPS, IRAOS, BSABS) used in formulating their content are as follows (*specific* symptoms are indicated by an asterisk):

C1. Worrying, nervousness or anxiety. [SOPS B1bc, D2] [IRAOS B.1. sections 2 and 3]
C2. Trouble with sleep or loss of appetite. [SOPS D1]
C3. Bodily restlessness, for example pacing up and down, not being able to sit still.
C4. Difficulty in coping with stress related to ordinary daily life events. [SOPS D4]
*C5. Difficulties thinking clearly or concentrating, interfering thoughts or thoughts interrupted. [SOPS A5, C3] [IRAOS B.1. section 4] [BSABS C.1.1. C.1.13.]
C6. Difficulties in considering alternatives or in making even minor decision.
*C7. Experience of thoughts running wild or difficulty in controlling the speed of thoughts. [SOPS A5b][BSABS C.1.3.]
*C8. Difficulties in understanding written text or speech heard. [SOPS C3] [BSABS C.1.6.]
C9. Depression, apathy, loss or energy or marked tiredness. [SOPS B2, B4, D2] [IRAOS B.1. section 5]
*C10. Difficulty in controlling one's speech, behaviour or facial expression while communicating. [BSABS A.7.2.]
C11. Difficulty or uncertainty in making contact with other people. [SOPS B.1.bc] [IRAOS B.1. section 6 and B.2. symptom 43] [BSABS A.7.1]
C12. Lack of initiative or difficulty in completing tasks. [SOPS B2]
C13. Social withdrawal, for example avoidance of company, feeling better in solitude. [SOPS B1] [IRAOS B.1. section 6]
*C14. Feeling that events in the environment or other people's behaviour specifically concern oneself. [SOPS A.1.d] [BSABS C.1.17]
*C15. Feeling euphoric or especially competent and important. [SOPS A3]
*C16. Disorders in connection with vision, such as blurred vision, visual oversensitivity or changing visual perceptions. [SOPS A.4.a] [BSABS C.2.2.,C.2.3. S2, C.2.8., C.2.9]
*C17. Disorders in connection with hearing, such as oversensitivity, hearing odd sounds or voices without obvious source. [SOPS A.4.de] [BSABS C.2.4.]
*C18. Difficulties in carrying out ordinary routine activities, such as washing, dressing, housework, cycling, or driving. [IRAOS 53] [BSABS C.3.3.]
*C19. Feeling that something strange or inexplicable is taking place in oneself or in one's environment. [SOPS A1d] [IRAOS B.1. section 12]
*C20. Feelings, thoughts or behaviours that could be considered weird or peculiar. [SOPS A1, C1, C2]
*C21. Feelings that one is being followed or being influenced in some special way. [SOPS A2][IRAOS B.1. sections 13 and 15]

The symptom criteria were formulated for both easy comprehension and inclusiveness to ensure wide coverage of reported morbidity. The symptom section covers both current (present during the last year) and lifetime presence (present earlier than the last year).

It was also considered reasonable to include behavioural symptoms in a separate section assessing general

functioning. This contains seven questions inquiring about current performance level and changes in performance during last year: general health, work performance, relations to close relatives, human relations more generally, leisure, self-care and household duties and attitudes of others towards the person him/herself. These items are rated on a four-point Likert scale: 'excellent/good/fair/poor' for current performance and 'worse/same/better/other' for change during last year.

The basis of evaluating the prod-screen

Assessing the predictive validity of a screening instrument for future psychotic conversion requires lengthy follow-up periods with large numbers of subjects because future psychosis is the actual target of the screening procedure. For the time being, we chose to assess the concordant validity of the screen by comparing screen diagnosis to an existing research instrument for evaluating prodromal symptomatology and diagnosis developed by Thomas McGlashan and his colleagues (Miller, 1999).

The Criteria of Prodromal Syndromes (COPS) is a composite set of three differentially defined prodromal syndromes, which are used to identify prodormal patients at relatively imminent risk for psychotic conversion. The COPS syndromes are:

- the presence of brief intermittent psychotic symptoms (BIPS);
- the presence of attenuated forms of positive symptoms (APS);
- genetic risk plus functional deterioriation.

They are used disjunctively – one can fulfil the criteria of one or several of the prodromal syndrome. The definitions formulated by McGlashan et al. (1998) are in principle similar to CAARMS criteria used by McGorry et al. (Yung 1996b).

To evaluate the presence of brief intermittent psychotic symptoms (BIPS) or attenuated psychotic symptoms (APS) the Scale of Prodromal Symptoms (SOPS) is used. The SOPS scale measures the strength of the following five positive psychotic symptoms on a seven-point Likert scale (absent/questionably present/mild/moderate/ moderately severe/severe but not psychotic/severe and psychotic):

- unusual thought content/delusional ideas;
- suspiciousness/persecutory ideas;
- grandiose ideas;
- perceptual abnormalities/ hallucinations; and
- conceptual disorganization.

According to the assumption made by the developers of the instrument, ratings from moderate to severe, but not psychotic, define the prodromal level of symptoms strength referred to as 'attenuated psychotic symptoms'.

The third syndrome 'genetic risk plus functional deterioriation' is defined by the conjunction of the presence of first-degree relatives with non-affective psychosis as a risk indicator for genetic influence and recent rapid decline in Global Assessment of Functioning (GAF) (Hall, 1995) score as an indicator of functional compromise. All in all, COPS criteria as defined by SOPS scale and using appropriate time frames are as follows:

- the presence of brief intermittent psychotic symptoms (SOPS level six symptoms with onset during the last three months and a frequency of once a month);
- the presence of attenuated forms of positive symptoms (SOPS level three to five symptoms with onset during the last year and a frequency of at least once a week during past month), and
- genetic risk plus functional deterioriation (first-degree relative of a schizophrenic patient or schizotypal personality disorder plus decrease of at least 30 GAF points for one month during the last year).

The definitions of COPS criteria have changed somewhat since the introduction to this instrument, and these definitions are according to an early version used for these studies reported in this article.

Finally, to enable structured interviewing of subjects, McGlashan et al. have developed the Structured Interview of Prodromal symptom (SIPS), which implements both COPS and SOPS in its structure but also measures negative, disorganizational and general symptoms.

Miller et al. (2002) have reported reliability and validity data on the SIPS interview. According to their data the SIPS has good inter-rater reliability in doing the diagnostic judgement whether a subject is prodromal or non-prodromal (kappa = 0.81; base rate

of prodromals in the study sample 39%) and high predictive validity: in their prediction study 54% of prodromal cases had developed schizophrenic psychosis at 12-month follow-up.

In the following studies, screen diagnosis with COPS criterion two (attenuated psychotic symptoms) is used as the gold standard of prodromal diagnosis. The recency criterion has been dropped and the concordant validity of PROD-screen diagnosis is measured against the presence of either lifetime or current presence of prodromal level symptomatology as measured by SIPS.

Methods

Initial face validity evaluation

To date, approximately 400 people have completed the PROD-screen questionnaire. The PROD-screen has proven easy to use and requires 20 to 30 minutes to complete by phone. Its acceptability has been very good. In a random sample of subjects in an unselected general population (GP sample described below) 64/75 (85%) interviewees reached by phone agreed to being interviewed by the screen.

Testing the screen for clinical construct validity

Subjects

Two samples were used for testing for the clinical construct validity of the PROD-screen: a general-population sample (GP sample) and patients from community mental health centres (CMHC sample). All subjects were interviewed using the screen, which examined their current functioning and the presence of symptoms during last 12 months.

The GP sample (n = 63) was formed by taking a random sample of 100 residents in Turku (age range 18 to 30) and contacting them by telephone for screening interview. Of them 25 persons could not be reached and further 11 persons declined to participate in the screening interview (refusal rate 15%). The sample consisted of 28 men and 35 women (the gender of one subject was not reported) and the mean age in the sample was 24.2 years (SD 3.66).

The CMHC-sample (n = 107) was collected from psychiatric outpatients in the Turku City Mental Health Centre. The workers in the outpatient units either gave the screens to the subjects for self-rating (n = 75) or interviewed the subjects with the screen (n = 30) (assessment method was missing for two subjects). Only patients who attended the policlinic for a new clinical episode, who had no prior history of psychosis, and who were not in an acute psychotic state were included. The refusal rate in this investigation is unknown. The CMHC-sample consisted of 35 men and 72 women, and the mean age in the sample was 29.9 (SD 11.3).

Results

The results of testing for clinical construct validity are shown in Table 1. According to the expectation, the sum scores of specific, non-specific and total symptoms were clearly lower in the GP sample than in the CMHC sample. Within samples, there were no gender or age differences. The current functional ability of subjects (sum score of the PROD-screen items B) was associated with higher scores of specific, non-specific and total symptom scores in both samples.

Testing the concordant validity of PROD-screen

Subjects

The concordant validity of the PROD-screen was tested in the DEEP research sample (DEEP sample). The DEEP sample (n = 132) was formed from a sample of non-psychotic subjects followed up in the DEEP study. The subjects were recruited from multiple sources:

- first-degree relatives of patients with schizophrenia or other psychoses (n = 44);
- psychiatric outpatients (n = 25);
- controls from an unselected general population sample (n = 34);
- volunteers, who were recruited through the local voluntary organization for relatives of psychiatric patients (n = 16); and
- adolescent inpatients and outpatients and their first-degree relatives (n = 13).

There were 43 men and 89 women in the sample with mean ages 32.5 (SD 9.0) and 33.1 (SD 10.3) respectively. The PROD-screen was administered to all the subjects in the DEEP sample by telephone and questioned as to their current functioning and the presence of symptoms during last 12 months. They later underwent a research interview which included:

- the socio-demographic background;

Table 1. PROD-screen scores by samples and subjects' background (ANOVA)

	Specific		Non-specific		Total	
	Mean	SD	Mean	SD	Mean	SD
General population						
(n = 64)	0.73	1.13	1.95	2.03	2.69	2.89
Gender						
Men (n = 28)	0.96	1.26	2.39	2.36	3.36	3.34
Women (n = 35)	0.57	1.01	1.63	1.72	2.20	2.44
p	*0.174*		*0.142*		*0.117*	
Age						
14–20 (n = 14)	1.00	1.36	2.50	2.14	3.50	3.16
20–30 (n = 50)	0.66	1.06	1.80	2.00	2.46	2.80
p	*0.324*		*0.259*		*0.237*	
Functional ability						
0–11 (n = 16; good)	0.38	0.50	0.88	1.02	1.25	1.34
12–14 (n = 26)	0.50	0.91	1.62	1.94	2.12	2.54
15–18 (n = 14)	1.07	1.64	2.71	2.16	3.79	3.56
19+ (n = 8; poor)	1.63	1.19	3.88	2.10	5.50	2.73
p	*0.026*		*0.001*		*0.001*	
CMHC patients						
(n = 107)	3.79	2.93	6.39	2.57	10.18	4.86
Gender						
Men (n = 35)	3.63	2.74	6.23	2.60	9.86	4.74
Women (n = 72)	3.86	3.04	6.47	2.56	10.33	4.94
p	*0.702*		*0.647*		*0.637*	
Age						
14–20 (n = 14)	3.21	3.17	6.00	2.94	9.21	5.22
20–30 (n = 64)	3.70	2.97	6.16	2.60	9.86	4.98
30–39 (n = 11)	4.55	3.30	6.82	1.78	11.36	4.23
40+ (n = 18)	4.06	2.46	7.28	2.49	11.33	4.54
p	*0.694*		*0.349*		*0.481*	
Functional ability						
0–11 (n = 8; good)	1.25	2.19	2.63	2.67	3.88	4.02
12–14 (n = 19)	2.47	2.44	4.84	3.00	7.32	4.99
15–18 (n = 32)	3.91	2.66	6.47	1.93	10.38	3.85
19+ (n = 48; poor)	4.65	3.04	7.58	1.74	12.23	4.14
p	*0.002*		*0.000*		*0.000*	
ANOVA: General population vs. CMHC patients (p)	*0.000*		*0.000*		*0.000*	

- SIPS (McGlashan, 1998); and
- SCID-I diagnostic interview (DSM-IV version).

This research interview and the PROD-screen interview were conducted independently.

The results were analysed both for the whole DEEP sample and separately for subsamples 1, 2 and 3. The entire sample was analysed together because of small numbers in subsamples, to give us a picture of the usefulness of screening in mixed samples, despite problems in interpreting the applicability of this result to different target populations. As it is, most ongoing longitudinal studies collect epidemiologically 'dirty' samples from multiple sources (Miller, 2002; McGorry,

2002). More detailed knowledge of its functioning in subjects from different epidemiological samples was derived from stratified analyses of the three subsamples.

As to collection of these sub-samples, sample 1 (the first degree relatives of patients with schizophrenia or other psychoses – FDRs) was collected by contacting the first degree relatives (siblings or children) of all schizophrenic patients discharged from Turku City Hospital during 1994 and 1995 (n = 183, of which 139 could be reached and 101 agreed to being interviewed). The total number of FDRs of these interviewees was 222 but in 24 cases contact was not permitted and 27 cases were outside the agreed age range (18 to 50). This gave us 172 FDRs to contact. Of these, 22% could not be reached and 9.9% denied screening, so we were able to screen on telephone 117 subjects altogether. From this group, we were able to interview 44 cases with SIPS, on which we have both screen and SIPS data. This is 33% of the total sample of the FDRs we were able to contact so refusal rate and selection is high in this sample and the generalizability of finding to FDRs of schizophrenia patients in general is questionable.

Sample 2, psychiatric outpatients (n=25), was collected from four outpatient policlinics of Turku Mental Health Centre and its sampling characteristics are not available.

Sample 3, controls from an unselected general population sample (n = 34), was collected by taking a random sample of residents in Turku (age range 18 to 50, n = 65), screening them by telephone and asking them to participate in a later SIPS interview. Of these 65 cases, eight were not reached, four had known psychosis and were not interviewed and further 17 refused. Of the remaining 36 subjects two failed to participate in the research interview (refusal rate 36%).

Results of DEEP sample analysis

The concordant validity of PROD-screen-specific symptoms for prodromal diagnosis was tested in the DEEP sample (n = 132) using data collected with the SIPS assessment (Miller, 1999). In the SIPS assessment, lifetime positive symptoms were divided into two categories of severity:

- symptomatic cases reaching severity level of two (n = 17) in some category of positive symptoms and
- prodromals having severity level from three to five (n = 39) in some category of positive symptoms .

The results of this analysis are depicted in Figure 1.

There was a proportional increase in SIPS prodromal cases up to the level of 3 to 4 scores in the PROD-screen. Because of small numbers, there was some variation in higher sum scores of the PROD-screen, but in general at that level and thereafter at least 60% of cases were prodromals. From the 39 lifetime prodromals, nine fulfilled the criteria of current prodromals according to the SIPS (Miller, 1999). All current prodromals had smaller scores than eight in PROD-screen; 7/9 (77.8%) of cases had from 2 to 7 and 2/9 (22.2 %) cases scores 0 or 1.

When the cut point was 2, sensitivity and specificity were reasonably good (Table 2). The sensitivity and specificity functions of screening are described with the ROC curve in Figure 2.

In this analysis, the area under curve (AUC) value is 0.793 (95% confidence limits 0.706 to 0.879).

From a practical point of view it is important to note that, with this choice of cut point (two specific symptoms), 80% of SIPS positive cases were detected by PROD-screen and the total group of subjects requiring further investigations was reduced by 60%. Depending on the purpose, other cut-points can also be chosen.

Results of analysis from stratified samples

To evaluate the accuracy of screening in different epidemiological populations, a stratified ROC analysis was undertaken from three subsamples (first degree relatives of schizophrenics, psychiatric outpatients, healthy controls). In the FDR sample AUC was 0.740 (95% confidence interval 0.543 to 0.937), so it seems that in this familial vulnerability group specific symptoms reasonably predicted SIPS status. In the healthy controls group the ROC curve was suggestive of being able to predict SIPS status but the result was not significant, (AUC = 0.624, [0.309:0.938]), possibly due to small sample size. In the outpatient sample the prodromal status was not predictive of SIPS status (AUC = 0.596, [0.368:0.825]). When interpreting this finding, it is important to notice that in both FDR and healthy controls samples, subjects reported a low level of symptoms compared to outpatient sample (0.75, SD 1.42 and 0.91, SD 1.75 versus 5.9, SD 2.64, significance level 0.000).

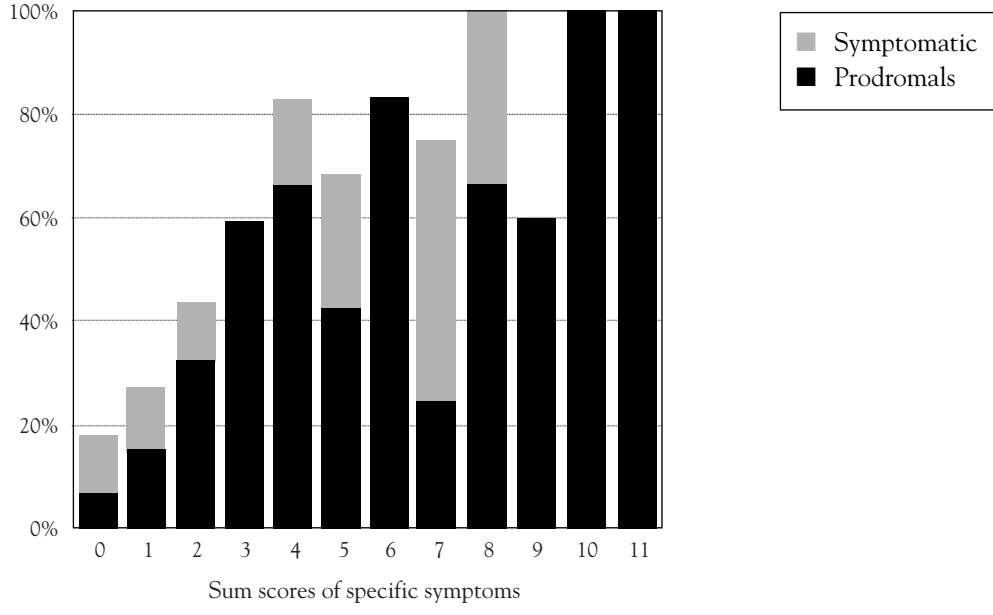


Figure 1: Prodromal and symptomatic cases according to sum scores of specific symptoms of the PROD-screen.

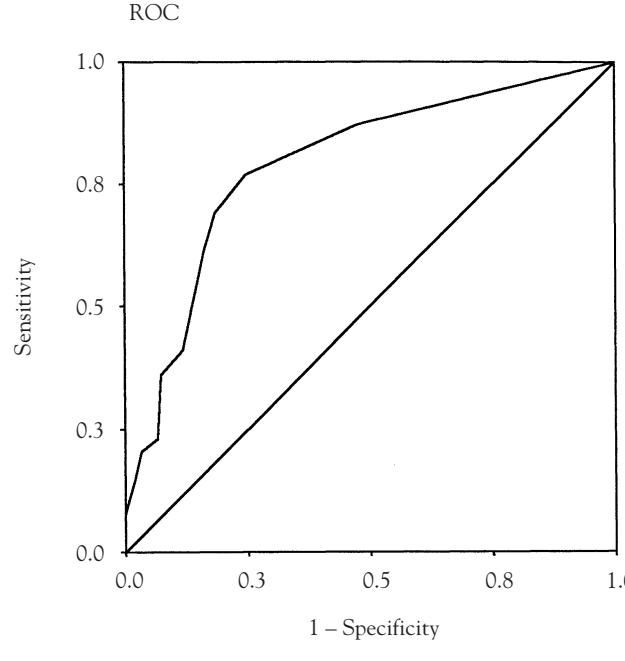
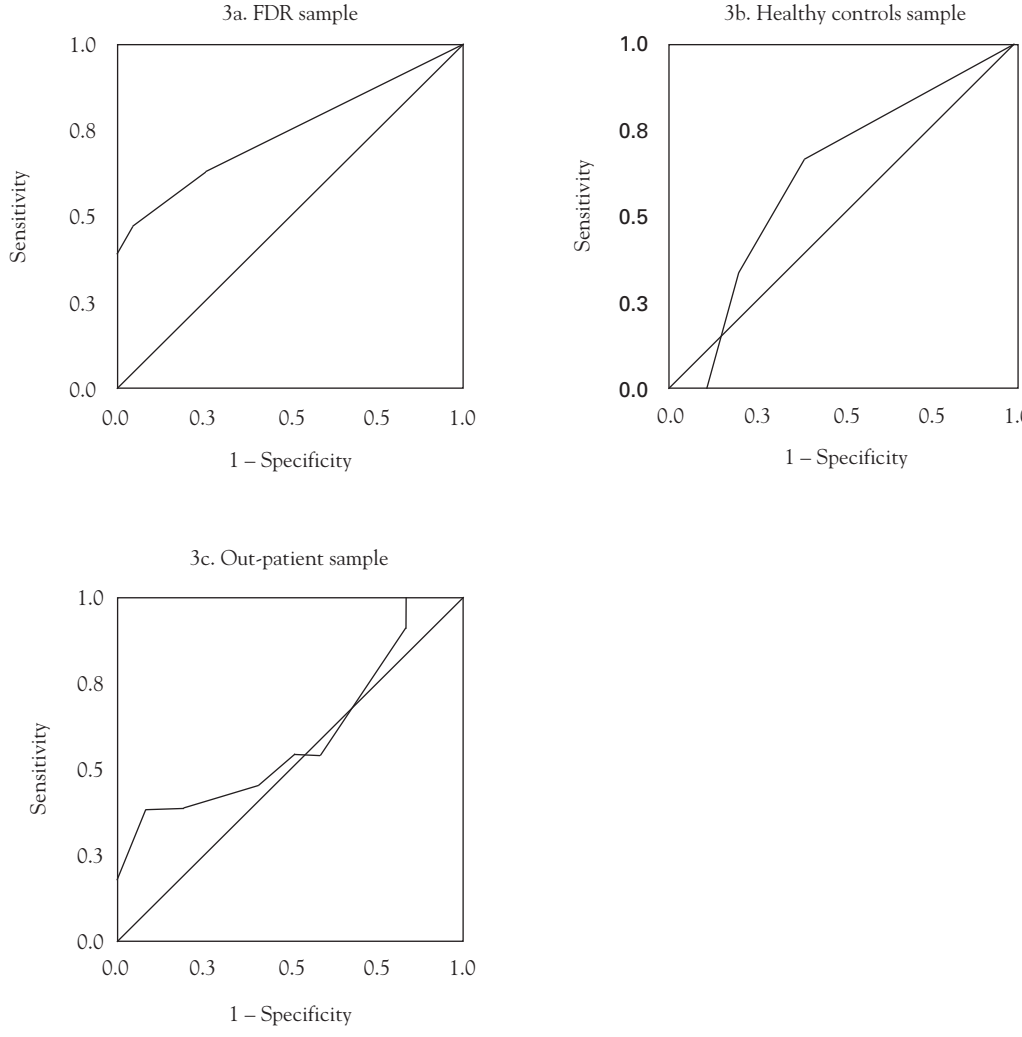


Figure 2. Specificity against sensitivity figures with the cut point 2 or more specific symptoms (ROC-analysis).

Table 2. Specificity and sensitivity of the PROD-screen

		Cut point 2 (0-1/2-11) PROD-screen					
		– (0–1)	+(2+)	All			
SIPS	–	70	23	93	*Specificity* *Sensitivity*	70/93 31/39	75.3 79.5
	+	8	31	39	*PPP* *NPP*	31/54 70/78	57.4 89.7
					OPP	101/132	76.5
	All	78	54	132			



Figures 3a-c. ROC analyses of the specificity and sensitivity of screen diagnosis in the FDR, healthy controls and out-patient samples.

Discussion

The central aim in this study was to develop a research instrument to identify prodromal stages of psychosis – one that would avoid large numbers of more extensive research interviews and would consequently enhance case detection for longitudinal studies.

As to the face validity of the PROD-screen, the attempt to identify subjects in the prodromal period of psychotic development by focusing on symptoms that have some resemblance to psychotic ones but that are clearly milder than typical psychotic symptoms is a reasonable strategy, considering what is known about the long and often insidious presentation of psychotic symptoms (Yung, 1996a).

Clinical construct validity refers to an assessment instrument's ability to distinguish cases manifesting clinically significant psychiatric symptomatology from those not doing so.

In this case, PROD-screen scores are clearly higher in clinical population (CMHC) compared to general population (GP), supporting the clinical significance of the symptomatology measured. High PROD-screen scores were also associated with high levels of reported decline in general functioning separately in both study populations, again suggesting that reported symptomatology is clinically relevant. Assuming that patient populations generally present with higher prevalence of prodromal symptoms than the general population, these findings support the construct validity of the instrument.

Concordant validity between PROD-screen and SIPS gold standard is used as a proxy for predictive validity, because assessing the predictive validity of the PROD-screen for psychotic conversion must await the completion of the DEEP follow-up study. For now we use concordant validity as a surrogate validation measure, which tells us to what extent PROD-screen agrees with our chosen gold standard for prodrome diagnosis.

The data presented here demonstrate concordant validity of the PROD-screen when this is evaluated using SIPS assessed prodromal diagnosis as golden standard. In a mixed sample of cases recruited from various sources PROD-screen gave correct classification in 77% of cases.

A cut point of two specific symptoms generated a sensitivity of 80%, where we would lose every fifth real positive subject in screening. A cut point of two also generates positive predictive power of 57%, meaning that almost three out of five subjects who screen positive would be true positives. In this case the overall predictive power would be fairly high, namely 77%.

If we chose the more stringent cut-off point of three specific symptoms present, the overall predictive power would be even higher, 79%. The sensitivity of the screening procedure would drop to 70% and we would be missing 3/10 real positive cases in screening. It is clear that the advantages and disadvantages of positive prediction power versus sensitivity will depend on the characteristics of the particular screening programme, but with an appropriate choice of cut-off criteria we can achieve moderate positive predictive power without compromising sensitivity.

This initial validity analysis of PROD-screen took place in a mixed sample of cases from different epidemiological populations, in which base rates for true prodromal states are most likely to vary very much. To obtain a better idea on the functioning of PROD-screen in different epidemiological samples, we carried out a stratified analysis in three epidemiological populations.

From this stratified analysis it emerged that, when screening first-degree relatives of schizophrenics, the PROD-screen score was a reasonably specific predictor of prodromality. Moreover, in the general population sample the screen functioned consistently, although due to small sample size this finding remained statistically insignificant.

When used in the clinical sample of psychiatric outpatients, the PROD-screen score did not differentiate between SIPS-positive and SIPS-negative cases, probably due to high levels of symptoms reported in this sample in general. This is a major drawback as clinical samples probably contain a higher base rate of true prodromal cases than general population samples. We have recently developed this screening method to take a more qualitative approach by including reports of verbal responses to symptom queries in the screen, and data on the validity of this modified screening procedure will be reported in the future.

It is noteworthy that we used only one of the COPS prodromal groups as the validity criterion. We used the attenuated psychotic symptom prodromal category as the validity criterion and felt it is reasonable for symptom-based screening. According to the Australian data (Thompson, 2001), the rate of conversion to psychosis in this subgroup (16/35, or 46%) was comparable to that from the entire sample

(41%), and in McGlashan's PRIME study all prodromal positive cases fulfilled this criterion (Miller, 2002).

The screen diagnosis was based on presence of symptoms during last year, and prodromal diagnosis was based on lifetime presence of prodromal states. We assumed that a short screening interview should concentrate on recent symptomatology to enhance the accuracy of symptom recall. For the purposes of predicting future risk of psychotic conversion, on the other hand, data on both lifetime and current symptom status are of interest. A relatively high ratio of prodromal positive cases only had prodromal symptomatology in the past (30/39, or 77%). As there was only one lifetime prodromal positive subject, who screened negative by the PROD-screen, it seems likely that it is sufficient to screen for only one year's presence of symptoms.

One obvious shortcoming with the present data is that the way screening was performed was not controlled: the data from the GP sample was collected entirely by phone and the MCHC sample by self-rating and by interview.

Conclusion

The PROD-screen is a useful instrument for screening for prodromal symptomatology both for self-rating and telephone interviews. With an appropriate choice of cut point it is able to detect the presence or absence of prodromal states with reasonable predictive power. According to our data, PROD-screen functions well with mixed samples and with first degree relatives of schizophrenic patients, and probably also with general population samples. In highly symptomatic populations like psychiatric outpatients, PROD-screen cannot distinguish SIPS prodromal syndromes and relevant modification are being developed.

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