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ORIGINAL PAPER

Predictors of psychosis: a 50-year follow-up of the Lundby population

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Abstract Behavioural and neuropsychological vulnerability have been associated with an increased risk of psychosis. We investigated whether certain clusters of premorbid behavioural and personality-related signs and symptoms were predictors of nonaffective and/or affective psychosis and schizophrenia, respectively, in a 50-year follow-up of an unselected general community population. Total population cohorts from the same catchment area in 1947 ($n = 2{,}503$) and 1957 ($n = 3{,}215$) that had been rated for behavioural items and enduring symptoms were followed up to 1997 regarding first-incidence of DSM-IV nonaffective and/or affective psychosis. Attrition was 1–6%. The influence of the background factors, aggregated in dichotomous variables (predictors), on time to occurrence of nonaffective and/or affective psychosis was assessed by means of Cox regression models. In multivariate models the predictors *nervous-tense*, *blunt-deteriorated*, *paranoid-schizotypal* and *tired-distracted* were significantly associated with subsequent nonaffective and/or affective psychosis. In simple models, *down-semidepressed*, *sensitive-frail* and *easily hurt* were significantly associated with development of psychosis. When schizophrenia was analysed separately *nervous-tense* remained significant in the multivariate model, although *blunt-deteriorated, paranoid-schizotypal* and *tired-distracted* did not; and *abnormal-antisocial* reached significance. To conclude, we found some evidence for anxiety-proneness, affective/cognitive blunting, poor concentration, personality cluster-A like traits and interpersonal sensitivity to be associated with general psychosis vulnerability.

Keywords Community population · Prospective study · Vulnerability · Nonaffective psychosis · Affective psychosis

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Introduction

Developmental, neuropsychological and behavioural vulnerability have been associated with the development of psychosis [7, 25, 27, 28, 39, 43, 44]. It is not known whether schizotypal, schizoid and avoidant personality traits are truly personality-related predictors (causal, pathoplastic or liability markers) or actually early illness signs of psychosis [33]. However, it might be that premorbid traits/signs lay closer to aetiological factors than frank psychosis does [34, 39, 40, 43].

Prospective studies on premorbid personality and personality-related background factors, and psychosis have been undertaken on army conscripts, national birth cohorts, high-risk samples and random general community samples (Table 1).

Findings reflect traits and signs from multiple domains; e.g. social anxiety, high neuroticism, low extraversion, emotional instability, schizotypal features, psychoticism and signs of neuropsychological deviance.

Premorbid behaviours and reports of various symptoms and the subsequent development of nonaffective and/or affective psychosis were assessed in the Lundby study, a prospective study of a total population 1947–1997. Since many identified risk factors for psychosis do not seem to be related to specific diagnostic categories but rather to their shared dimensions [22, 42, 43] and to increase sample size, nonaffective and/or affective psychosis was defined as a group of diagnoses that share psychotic symptoms and have unknown aetiopathologies.

Based upon the studies in Table 1, we hypothesized that nonaffective and/or affective psychosis may be predicted by clinically assessed behaviours and subjective experiences such as: interpersonal sensitivity, anxiety-proneness, affective instability, low mood, affective blunting/anhedonia, immaturity, forgetfulness, tiredness/distractibility, abnormal social behaviours and cluster-A like traits (e.g. suspiciousness, aloofness, oddness, eccentricity).

Methods

Sample

All individuals ($n = 2{,}550$; males 1,312, females 1,238) in a rural catchment area in the south of Sweden were included in the Lundby study in 1947 (the 1947 cohort). In 1957, 1,013 newcomers to the area (males 511, females 502) were added, but since 253 had died (males 128, females 125) between 1947 and 1957, there were 3,310 individuals (the 1957 cohort) in the study in 1957 (males 1,696, females 1,614) (including those who had left the Lundby area). There have been three follow-ups, regardless of residence; in 1957, 1972 ($n = 2{,}827$; males 1,425, females 1,402) and 1997 ($n = 1{,}797$; males 851, females 946). At all investigations, observations of clinical and subclinical behaviours, and the probands' subjective report on various personality-related items were scored at personal interviews conducted by psychiatrists. The interviews contained itemized checklists of behaviours and subjective reports. Other sources of information were registers (e.g. the national patient register and regional archives), case notes (e.g. psychiatric and other clinics and records of general practitioners) and key-informants (e.g. relatives). Attrition was 1–6% since sufficient information for psychiatric evaluations could be obtained in 99% of the subjects in 1947–1972, and in 94% in 1972–1997.

Those suffering from any psychotic disorder or dementia at the beginning of the study period were excluded from the calculations. Median age of psychosis onset for the excluded probands was 29 years (q1 21 years, q3 35 years). Thus, in the 1947 and 1957 cohorts there were 2,503 (males 1,292, females 1,211) and 3,215 (males 1,651, females 1,564) probands, respectively under risk for psychotic disorder. The cohorts overlap; 2,220 probands (males 1,148, females 1,072) are members of both.

The cohorts had similar age distributions. In 1947 the median age was 34 years (lower and upper quartiles 15–51, range 0–92). In 1957 the median age was 33 years (lower and upper quartile 18–51, range 0–96). Slightly fewer probands were married and divorced in 1947 (45.7 and 0.7%, respectively) than in 1957 (50.2 and 1.5%, respectively). The proportion of widowed probands in 1947 and 1957 were similar (4.8 and 4.5%, respectively). The socioeconomic status had changed somewhat from 1947 to 1957 in that fewer probands were white collar workers in 1947 (6.7%) than in 1957 (12.1%), more were self-employed (including farmers) in 1947 (18.7%) than in 1957 (15.5%) but the proportion of blue collar workers were similar in 1947 (49.5%) and 1957 (49.8%). Between 1947 and 1972, the Lundby area had become suburban and many of the subjects had moved to the neighbouring cities or other parts of Sweden [13, 30]. Details about the sample, the interviews, the supplementary data-sources, and the attrition have been published elsewhere [30].

The ethics committee of Lund university hospital approved the 1997 follow-up of the Lundby Study. Participants provided written consent.

Assessment of psychotic disorder

In 1947 mental disorders were diagnosed according to Essen-Möller [11]. However, at the follow-up in 1957 and subsequently a revised diagnostic system was used [14]; the 1947 diagnoses were re-diagnosed according to this. According to the Lundby 1957-classification "psychosis" is characterized as a psychopathological state of which the individual lacks adequate insight and suffers from hallucinations, delusions, formal thought disorder, manic behaviour, catatonia or confusion. However, psychosis part of a depressive episode is diagnosed as "depression plus other psychiatric symptoms", meaning that depression with psychotic features is not included in Lundby "psychosis." A detailed description of the Lundby classification has been published elsewhere [12]. At the 1997 follow-up, DSM-IV diagnoses [1] were assessed in parallel with

Table 1 Prospective studies on premorbid personality traits and personality-related background factors and psychosis

Investigator/project	Sample (*n*), mean age	T1–T2 (years)	Psychosis criteria	Significant predictors
Malmberg et al. [26]	Male army conscripts (50,087), 18–20 years	15	Schizophrenia and other psychoses, ICD-8	Poor social adjustment and interpersonal difficulties reflecting social anxiety (e.g. feeling more sensitive than others)
Jones et al. [20]	National birth cohort (5,362), 4–15 years	27–39	Schizophrenia and Schizo-affective disorder, DSM-III-R	Solitary play preference, anxiety in social interaction and speech problems
Van Os et al. [41]	National birth cohort (5,362), 16 years	27	Schizophrenia, DSM-III-R	High neuroticism and low extraversion
The National Child Development Study [9]	National birth cohort (153,989), 7–11 years	16–28	Narrow schizophrenia, PSE-CATEGO	Higher scores on over-reactive externalizing behaviour, e.g. hostility and inconsequential behaviour, in boys at 7 and 11 years; in girls at 7 years. Higher scores of under-reactive internalizing behaviour, e.g. withdrawal and depression, in girls at 11 years
The Dunedin Multidisciplinary Health and Development Study [5]	Unselected general population birth cohort (1,037), 3–11 years	23	Psychotic symptoms, diagnostic interview schedule for children (age 11 years) "Schizophreniform disorder", DSM-IV (age 26 years)	Internalizing problems (e.g. worrying, appearing unhappy), peer rejection, impairments in verbal comprehension, and cognitive impairment predicted psychotic symptoms at age 11 years and "schizophreniform disorder" at 26 years. Self-reported psychotic symptoms at age 11 years predicted "schizophreniform disorder" at 26 years
Ekstrøm et al. [10]	Mixed high-risk sample (265), 12 years	19–21	Schiz-spectrum, DSM-III-R	Lower scores on intelligence, concentration, maturity, friendliness and cooperation. Higher scores on emotional instability, aggression
Schiffman et al. [37]	As above	19–21	Schiz-spectrum, DSM-III-R	Socio-behavioural deficits
The Copenhagen High-Risk Project [33]	High-risk sample (207), 15 years	10	Schiz-spectrum, DSM III	As babies passive with short attention spans. In school isolated, rejected, disturbing behaviour, poor affective control. At 15 years abnormal emotional rapport (e.g. tense, peculiar, guarded, introverted), formal cognitive disturbance (e.g. unconcentrated, preoccupied)
The Copenhagen High-Risk Project [6]	As above	25	Schizophrenia, DSM-III-R	Unusual thoughts-experiences and psychoticism
The New York High-Risk Project [2]	Mixed high-risk sample (185), 9.48 years	23	Schizophrenia-related psychoses, RDC	Externalizing behaviours (e.g. discipline problems, difficulties to get along with brothers and sisters, fights, temper tantrums)
The Edinburgh High-Risk Study [19]	High-risk sample (199), 16–24 years	10	Schizophrenia, ICD-10	Social anxiety, withdrawal and other schizotypal features
The Helsinki High-Risk Study [30]	High-risk sample (258), pre-school (<7 years) and school age (7–17 years)	35–39	Schiz-spectrum and other psychoses, DSM-IV-TR	Social adjustment problems (spectrum disorders)
The Philadelphia Cohort of the National Collaborative Perinatal Project [3]	Population cohort (9,236), 8 months–7 years	29–36	Schizophrenia and Schizo-affective disorder, DSM-IV	At 4 years focal deviant behaviours (e.g. meaningless laughter, excessive crying, echolalia). At 7 years focal deviant behaviours and social maladjustment (e.g. deviances in emotional reactivity, duration of attention span, rapport, assertiveness and speech intelligibility)
The Nemesis Study [24]	Community sample (3,929), 41.5 years	3	Psychosis, BPRS-rated	High neuroticism

Lundby diagnoses for the period 1972–1997. The diagnoses were set jointly by the research team [30].

In 1997, to achieve comparability of diagnoses for the whole study period, a DSM-IV evaluation of cases with Lundby "psychosis" and "depression plus other psychiatric symptoms" was made, in retrospect for the period 1947–1972. All cases 1947–1997 were then assigned to five DSM-IV groups: (a) psychosis due to a general medical condition, (b) substance-induced psychotic disorder including substance-induced delirium/intoxication with psychotic features, (c) schizophrenia and schizoaffective disorder, (d) other non-affective psychotic disorders and (e) affective psychotic disorder. Group (a) and (b) were excluded since the causes of them are assumed to be known. Two outcome categories were constructed by collapsing group c–e (nonaffective and/or affective psychosis) and analysing separately group c (schizophrenia/schizoaffective disorder).

Cases of first-incident nonaffective and/or affective psychosis

Between 1947 and 1997, there were 61 cases of first-incident nonaffective and/or affective psychosis (Table 2). Forty-five belonged to the 1947-cohort (male 17, female 28) and 42 belonged to the 1957-cohort (male 22, female 20). Twenty-six cases belonged to both cohorts. Median age at onset was 46.0 years; lower quartile was 30.5 and upper 64.0 years.

Assessment of various premorbid behavioural traits and symptoms

At interviews in 1947, 1957 and 1972 psychiatrists rated observable behaviours in probands (e.g. affective and vegetative reactions) such as: tension, gloominess, torpidity, aloofness and sensitivity [12]; the ratings were: absent, indicated, evident or extreme. Furthermore, structured questions were put to the probands about their subjective opinion of various personal lifelong habitual dispositions/symptoms (also mostly related to affect), e.g.: "Are You nervously disposed?", "Do You cry easily?", "Do You often feel unjustly treated?", "Are You sensitive to unpleasant things?" and "Do You get tired easily?"; the answers to these questions [12], were given as: never, seldom, sometimes or often.

After the interviews, the psychiatrists dichotomously assessed some constellations of the observed behaviours and the reported symptoms (in the following called *integrated items*) such as schizoid and abnormal personality. Essen-Möller wrote in 1956 about schizoid personality: "probably related to schizophrenia or to schizophrenic taint", with traits like: "lowered accessibility or flexibility, dryness, brittleness" and "tenseness" [11]. The schizoid personality concept used was influenced by Bleuler [4], i.e. tendency to seclusion, withdrawal and irritability. Abnormal personality referred to psychopathy according to Schneider, i.e. individuals behaving in socially abnormal ways in the absence of mental retardation or mental illness, e.g. displaying gloominess, stickiness, dysphoria, overactivity, suspiciousness or aggression [14, 38].

Based on the observed behaviours, reported symptoms and integrated items dichotomous predictors were constructed. The predictors are shown in Table 3 together with their corresponding originally observed behaviours, reported symptoms and integrated items, and the years in which they were assessed. The distributions by age of the predictors, and the psychotic disorder groups, in the cohorts are presented in Table 4.

Time between predictor assessment and psychosis onset

In the probands who developed nonaffective and/or affective psychosis, the years from the first assessment of

Table 2 Cases of first-incident nonaffective and/or affective psychosis 1947–1997

	Males $n = 29$	Females $n = 32$	Total $n = 61$
Nonaffective psychosis	18	24	42
Schizophrenia	9	8	17
Paranoid	8	7	15
Catatonic	1	–	1
Undifferentiated	1	–	1
Other nonaffective psychosis	9	16	25
Delusional disorder	5	6	11
Brief psychotic disorder	1	3	4
Psychotic disorder NOS	3	7	10
Affective psychosis	11	8	19
Bipolar	6	3	9
Depressive	5	5	10

Table 3 Observed behaviours, reported symptoms and integrated items grouped into predictor variables

Predictor variables	Original items scored by interviewer or self-reported	Assessment years
Nervous-tense	Tense[a], restless[a], insecure[a], strained[a], vegetative[a], lachrymose[a], worried[b], nervous[b], tense[b], susceptible to adversity[b], vegetative[b], cries easily[b], difficulty to collect one's thoughts[b]	1947, 1957, 1972
Down-semidepressed	Heavy[a], gloomy[a], semi-depressed[a], Down[b]	
Blunt-deteriorated	Torpid[a], blunt[a], empty[a], intellectually deteriorated[a], disturbed memory[a]	
Paranoid-schizotypal	Paranoid[a], schizoid[c] (unresponsive, reserved, aloof), bizarre[a]	
Abnormal-antisocial	Suspicious[c], hyperthymic[c], fanatic[c], indolent[c], emotionally labile[c], aggressive[c], explosive[c]	
Immature-primitive	Emotionally immature[a], undifferentiated[a], primitive[a]	
Sensitive-frail	Sensitive[a], brittle[a], frail[a]	1957, 1972
Easily hurt	Difficulty forgetting being wronged[b], feels unjustly treated[b]	
Affective lability	Affectively labile[a]	
Forgetful	Forgetful[b]	
Tired-distracted	Tired[a], poorly concentrated[a], tires easily[b]	

[a] Behaviours: assessed by interviewer, judged to be personality-related, not situation-specific and not an expression of clinical disorder

[b] Reported symptoms: self-reported enduring characteristic

[c] Integrated items: constellations of observed behaviour and reported symptoms assessed by interviewer: schizoid personality [4, 11], and subgroups of psychopathy according to Schneider [38]

the predictors to psychosis was analysed to see if the predictors were usually associated with imminent illness onset, which would make the predictors likely to reflect early signs of the prodrome of the psychotic disorder, or if the earliest predictor assessments were clearly separated in time from psychosis onset, which would suggest the predictors to be more likely to reflect personality-related premorbid characteristics and/or early fluctuating non-psychotic states on the pathway to psychosis (Table 5).

The construction of the predictors for the present paper was not an attempt to create an inventory of personality for general use; it was merely meant to cluster a large amount of inter-related potential risk factors for psychosis accumulated over 25 years at three interviews conducted by different interviewers into a manageable set of variables. Further, although the original assessments of the items were aimed at rating stable personality-related behaviours and symptoms it is more likely that the ratings were a blend of enduring traits and fluctuating affective state variables, since it was not uncommon for the assessments of the items to change from one interview to another (e.g. a proband could be assessed as nervously disposed at one interview but not at next).

Statistical analysis

To reduce the many premorbid original items (observed behaviours, reported symptoms and integrated items; see Table 3) we used factor analysis together with consensus decisions in the research team. In the consensus group the final decisions were taken which clinically related items were to be grouped together. For each set of items that were eventually grouped together a dichotomous predictor was constructed indicating either absence or low severity in all the original items of the set, or medium-high severity in at least one item.

As the predictors may fluctuate they were time-dependent in the analysis, thus allowing for them to change value during follow-up. The observed behaviours, reported symptoms and integrated items which were assessed at the interviews in 1947, 1957 and 1972, and from which the predictors were constructed, could in the analysis change their values only at these dates; consequently the predictors were regarded as constant between the cut-off dates.

The influence of the constructed predictors on time to occurrence of nonaffective and/or affective psychotic disorder and schizophrenia, respectively, was assessed by means of Cox regression models. Censoring occurred in cases of death, dementia, refusal to continue or the end of the study. Some variables were added on the interview checklists in 1957.

In order to utilize all information separate regression analyses for the 1947 and 1957 cohorts were carried out. First, the influence of each predictor was assessed in simple models adjusting for age and sex by including age and sex in each simple predictor model.

Table 4 Distributions of first assessments of predictors and disorders according to age-groups

	0–14 years	15–44 years	45–64 years	65+ years	0+ years
1947 cohort, $N = 2{,}503$					
Predictors (%)					
Nervous-tense	3.6	28.8	15.5	6.3	54.2
Down/semi-depressed	0.1	1.8	2.2	1.0	5.1
Blunt-deteriorated	0.4	5.4	2.3	1.3	9.4
Paranoid-schizotypal	0.1	5.9	4.4	2.9	13.3
Abnormal antisocial	0.4	4.2	2.3	1.5	8.4
Immature-primitive	0.3	3.4	2.4	1.1	7.1
Disorders (*N*)					
Nonaffective and/or affective psychosis	0	18	15	13	45[b]
Schizophrenia	0	8	4	2	14
Other nonaffective psychosis	0	8	3	6	17
Affective psychosis	0	2	8	5	15
1957 cohort, $N = 3{,}215$					
Predictors (%)					
Nervous-tense	1.8	23.1	14.2	4.9	44.1
Down/semi-depressed	0	1.1	1.3	0.7	3.1
Blunt-deteriorated	0	1.5	1.1	1.2	3.7
Paranoid-schizotypal	0	2.7	2.6	1.7	7.0
Abnormal antisocial	0	3.4	1.1	0.6	5.2
Immature-primitive	0	2.7	2.2	0.8	5.8
Sensitive-frail[a]	0	4.6	3.2	1.5	9.4
Easily hurt[a]	0	4.7	4.5	1.6	10.9
Affective lability[a]	0.3	4.4	2.9	1.0	8.7
Forgetful[a]	0	0.5	1.1	3.1	4.7
Tired-distracted[a]	0.1	9.9	10.0	6.6	26.6
Disorders (*N*)					
Nonaffective and/or affective psychosis	1	19	10	12	42
Schizophrenia	0	7	2	1	10
Other nonaffective psychosis	0	9	4	8	21
Affective psychosis	1	3	4	3	11

[a] Not assessed in 1947

[b] One subject had two disorders; first other NAP, and then schizophrenia

Second, to see whether the influence of the predictors differed significantly between the sexes, a sex × predictor interaction term was included in simple models. Third, to see whether the influence of the predictors differed by age, an age × predictor interaction term was included in simple models. Fourth, multivariate models were obtained starting with models including all predictors, followed by a backward, step-wise regression procedure, in which the predictors with the highest P values were removed from the model, one at each step. The multivariate models were adjusted for age and sex by keeping these covariates in the final models. P values <0.05 indicated statistical significance. Ninety-five percent confidence intervals (CI) were calculated. SPSS for Windows, version 13.0, was used for the calculations.

Results

Cox regression

Simple and multivariate analysis, all subjects, nonaffective and/or affective psychosis 1947–1997 and 1957–1997 (Table 6). In the 1947 cohort, in both the simple and multivariate models, the predictors *nervous-tense* and *blunt-deteriorated* were significantly associated with the

Table 5 Time (years) between earliest positive assessment of predictors in future cases and onset of nonaffective and/or affective psychosis

	md (q1–q3)	*n*
Nervous-tense	10.3 (5.2–22.4)	38
Down/semi-depressed	11.3 (0.8–22.2)	3
Blunt-deteriorated	9.3 (5.9–21.5)	8
Paranoid-schizotypal	13.2 (2.9–25.8)	11
Abnormal antisocial	10.2 (3.7–25.3)	8
Immature-primitive	19.1 (9.5–27.0)	4
Sensitive-frail	10.3 (7.8–22.2)	7
Easily hurt	11.9 (9.6–14.0)	7
Affective lability	5 (0.2–0.8)	2
Forgetful	5.2 (0.8–9.6)	2
Tired-distracted	11.6 (8.6–12.8)	14

md Median, *q* quartile, *n* number of cases

outcome psychosis, having hazard ratios of roughly 2 and 4, respectively. Moreover, in the simple model of the 1947 cohort, the predictor *abnormal-antisocial* had a hazard ratio of 2.76 ($P = 0.06$); but, nevertheless, in the multivariate model 1947–1997 the association between *abnormal-antisocial* and emerging nonaffective and/or affective psychosis disappeared.

In the 1957 cohort, in both the simple and final multivariate models, the predictors *nervous-tense*, *paranoid-schizotypal* and *tired-distracted* were significantly associated with incident psychosis; *nervous-tense* with a hazard ratio of 2.84 in the simple model and 2.38 in the final multivariate model; *paranoid-schizotypal* with a hazard ratio 4.45 in the simple model and 5.03 in the final multivariate model; and *tired-distracted* with a hazard ratio of 2.93 in the simple model and 2.35 in the multivariate model. Moreover, in the simple models of the 1957 cohort, the predictors *down-semidepressed* (hazard ratio 4.40), *easily hurt* (hazard ratio 2.63) and *sensitive-frail* (hazard ratio 2.76) were significantly associated with psychosis but none of them reached significance in the final multivariate model of the 1957 cohort.

Sex–predictor interactions

Only one predictor, *nervous-tense*, and only in the 1947 cohort was differently associated with the hazard ratio of psychosis in males and females. In the 1947 male simple

Table 6 Cox regression models, simple and multivariate, for nonaffective and/or affective psychosis in the Lundby 1947- and 1957-cohorts, hazard ratios, 95% confidence intervals and *P* values

Predictor	1947 Cohort		1957 Cohort	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Simple models[a]				
Nervous-tense	2.27 (1.24–4.17)	0.008	2.84 (1.52–5.32)	0.001
Down-semidepressed	2.23 (0.54–9.31)	0.27	4.40 (1.34–14.48)	0.02
Blunt-deteriorated	4.15 (1.72–10.02)	0.002	2.80 (0.67–11.71)	0.16
Paranoid-schizotypal	2.10 (0.81–5.45)	0.13	4.45 (1.85–10.68)	0.001
Abnormal-antisocial	2.76 (0.97–7.84)	0.06	2.18 (0.66–7.13)	0.20
Immature-primitive	1.29 (0.31–5.38)	0.72	1.27 (0.30–5.30)	0.74
Sensitive-frail[b]	–	–	2.76 (1.13–6.78)	0.03
Easily hurt[b]	–	–	2.63 (1.08–6.38)	0.03
Affective lability[b]	–	–	0.84 (0.20–3.50)	0.81
Forgetful[b]	–	–	3.10 (0.72–13.36)	0.13
Tired-distracted[b]	–	–	2.93 (1.46–5.90)	0.003
Multivariate model[c]				
Age	1.00 (0.99–1.02)	0.61	0.99 (0.97–1.01)	0.35
Sex	1.51 (0.81–2.80)	0.19	0.73 (0.39–1.36)	0.32
Nervous-tense	2.31 (1.26–4.25)	0.007	2.38 (1.23–4.61)	0.01
Blunt-deteriorated	4.29 (1.78–10.34)	0.001	–	NS
Paranoid-schizotypal	–	NS	5.03 (2.09–12.01)	<0.001
Tired-distracted[b]	–	–	2.35 (1.13–4.86)	0.02

HR hazard ratio, *CI* confidence interval, *NS* not significant

[a] Adjusted for age and sex

[b] Not assessed in 1947

[c] $P = 0.05$ was the threshold for statistical significance in the regression procedure

model the hazard ratio of *nervous-tense* was 5.52 (95%CI 2.06–14.75, *P* value 0.001). In the 1947 female simple model the hazard ratio was 1.31 (95%CI 0.62–2.77, *P* value 0.48). In the 1947 male multivariate model the hazard ratio was 5.54 (95%CI 2.07–14.82, *P* value 0.001). In the 1947 female multivariate model the hazard ratio was 1.32 (95%CI 0.63–2.80, *P* value 0.46).

Age–predictor interactions

Only one predictor in the 1957 cohort, *tired-distracted*, interacted with age. The hazard ratio of *age* × *tired-distracted* was 1.04 (95%CI 1.00–1.08, *P* value 0.041).

Simple and multivariate analysis, all subjects, schizophrenia 1947–1997 and 1957–1997 (Table 7). When schizophrenia was analysed separately (excluding other nonaffective psychoses and affective psychoses) *nervous-tense* remained significant in the simple and multivariate models of the 1957 cohort, but did not reach significance in the 1947 cohort. *Abnormal-antisocial* reached significance in the simple and multivariate models of the 1947 cohort, but not in the 1957 cohort. *Blunt-deteriorated, paranoid-schizotypal* and *tired-distracted* were not significantly associated with schizophrenia, although *blunt-deteriorated* almost reached significance in the simple model of the 1947 cohort ($P = 0.059$).

Discussion

We sought to find clinically assessed premorbid behavioural and personality related background factors that were associated with an increased risk of developing nonaffective and/or affective psychotic disorder in a community sample. In simple and multivariate analyses we found that factors clustered in various dichotomous predictors were significantly associated with a subsequent onset of psychosis. The predictors were: *nervous-tense* (sharing some features with high neuroticism and the anxious/fearful traits of DSM-IV cluster C), *down-semidepressed*, *blunt-deteriorated* (sharing some features with the negative symptom dimension in schizophrenia—affective blunting, impoverished thinking and avolition), *paranoid-schizotypal* (sharing some features with the suspicious/odd/eccentric DSM-IV cluster-A traits), *sensitive-frail*, *easily hurt* and *tired-distracted*.

Our results support findings from earlier studies; from retrospective studies that neurotic, schizoid, paranoid and

Table 7 Cox regression models, simple and multivariate, for schizophrenia in the Lundby 1947 and 1957 cohorts, hazard ratios, 95% confidence intervals and *P* values

Predictor	1947 cohort		1957 cohort	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Simple models[a]				
Nervous-tense	1.94 (0.63–5.97)	0.245	5.56 (1.53–20.22)	0.009
Down-semidepressed	0.00 (0.00–)	0.983	0.00 (0.00–)	0.985
Blunt-deteriorated	4.43 (0.95–20.73)	0.059	0.00 (0.00–)	0.985
Paranoid-schizotypal	3.66 (0.76–17.66)	0.105	3.38 (0.42–27.34)	0.253
Abnormal-antisocial	9.49 (2.52–35.67)	0.001	2.99 (0.37–24.02)	0.304
Immature-primitive	0.00 (0.00–)	0.985	0.00 (0.00–)	0.986
Sensitive-frail[b]	–	–	2.14 (0.26–17.89)	0.483
Easily hurt[b]	–	–	0.00 (0.00–)	0.981
Affective lability[b]	–	–	0.00 (0.00–)	0.983
Forgetful[b]	–	–	0.00 (0.00–)	0.985
Tired-distracted[b]	–	–	3.41 (0.76–15.24)	0.109
Multivariate model[c]				
Age	0.98 (0.95–1.01)	0.227	0.96 (0.92–1.00)	0.058
Sex	1.72 (0.58–5.09)	0.324	0.66 (0.20–2.21)	0.504
Nervous-tense	–	NS	5.56 (1.53–20.22)	0.009
Abnormal-antisocial	9.49 (2.52–35.67)	0.001	–	NS

HR hazard ratio, *CI* confidence interval, *NS* not significant

[a] Adjusted for age and sex

[b] Not assessed in 1947

[c] $P = 0.05$ was the threshold for statistical significance in the regression procedure

schizotypal traits are associated with psychosis vulnerability [8, 36]; from high-risk studies that anxiety, tension, social sensitivity, suspiciousness and schizotypal traits and concentration deficits are associated with psychosis vulnerability [2, 6, 10, 19, 31, 34, 37]; and from community prospective studies that impaired emotional reactivity, impaired attention and anxiety and other traits of neuroticism are associated with psychosis vulnerability [3, 24]. Our results were also consistent with findings from studies on prodromal symptoms of psychosis in that anxiety and depression often precedes a psychosis development and that negative symptoms, concentrations problems and distrust and withdrawal are common during the prodromal phase [17, 45].

The median age of onset of nonaffective and/or affective psychosis in the study was high (md 46 years, q1 30.5 years, q3 64 years). The high age of onset distribution may be explained by selection of late onset cases among the probands under risk for psychotic disorder due to biased exclusion of already affected early onset cases ($n = 39$) at the intakes and a long follow-up period. The age of psychosis onset was lower among the excluded probands (md 29 years, q1 21 years, q3 35 years).

Nervous-tense

Being assessed as *nervous-tense* roughly doubled the risk of developing a psychotic disorder in both of our cohorts. This accords with the finding in the British 1946 birth cohort that cases who later developed schizophrenia at age 15 were rated by teachers as anxious in social situations [20] and at age 16 years scored high on neuroticism [41]. It also accords with the finding in the Nemesis Study that neuroticism in adults increased the risk for development of psychotic symptoms [24]. Neuroticism is related to stress vulnerability, anxiety proneness and autonomic instability [16, 32]. Our construct *nervous-tense*, consisting of items like *susceptible to adversity, insecure, worried, tense* and *vegetative*, share some features with neuroticism. Further, in the Edinburgh High-Risk Study anxiety-depression at age 16 years was associated with an increased risk of developing schizophrenia in high-risk individuals compared to controls as well as to high-risk individuals who had not developed any symptoms [19]. The finding is also consistent with the finding that anxiety is common during the prodromal phase of schizophrenia [15, 17, 45]. The results provide evidence for a relationship between anxiety proneness and psychosis vulnerability. An interesting finding was that *nervous-tense* was significantly associated with psychosis vulnerability in males but not females in the 1947 cohort. One possible explanation may be that the male group who reported and/or showed signs of nervousness and tension was more severely afflicted than the corresponding female group, due to culturally conditioned reluctance in males to express feelings of this kind.

Down-semidepressed

Being assessed as *down-semidepressed* roughly quadrupled the risk of developing a psychotic disorder, but only in the simple model of the 1957 cohort. This finding may approximately accord with the finding in the British 1946 birth cohort that solitary play preference at age 4–6 years [20] and low extraversion at 16 years [41] predicted schizophrenia. It also accords with the under-reactive behaviour found in preschizophrenic girls in the National Child Development Study [9] and in the children of the Dunedin Multidisciplinary Health and Development Study who developed psychotic symptoms and schizophreniform disorder [5]. Furthermore, it is consistent with findings that depressive symptoms are common during the prodromal phase of schizophrenia [15, 17, 45]. This would accord with the increased reported anhedonia that occurs across all at-risk groups of schizophrenia: those at familial high risk, those with schizotypal characteristics and those in the putative prodrome to psychosis [35].

Blunt-deteriorated

Being assessed as *blunt-deteriorated* roughly quadrupled the risk of developing a psychotic disorder, but only in the 1947 cohort. This accords with the findings from the Copenhagen High-Risk Project, in which was found an association between abnormal emotional rapport at age 15 years and later development of schizophrenia [34]. Even though not replicated in the 1957 cohort our result provide some evidence for negative and cognitive symptoms being associated with psychosis vulnerability.

Paranoid-schizotypal

Being assessed as *paranoid-schizotypal* increased the risk of developing a psychotic disorder four to five times, but only in the 1957 cohort. This accords with findings from family studies that there is an increased frequency of schizotypal, paranoid and schizoid personality disorder in relatives of probands with schizophrenia; an increased frequency of schizotypal personality disorder in relatives of probands with other nonaffective psychotic disorders; and an increased frequency of paranoid personality disorder in relatives of probands with schizo-affective disorder [23]. It also accords with the finding that schizophrenia patients retrospectively fulfilled criteria of premorbid personality disorder in 85% of the cases, encompassing, amongst others, the cluster A (schizoid, paranoid and schizotypal) personality disorders [36]. Furthermore, the result accords

with the findings from the Copenhagen High-Risk Project that individuals who went on to develop schizophrenia at 15 years of age were assessed as e.g. peculiar, guarded, introverted [34] and that they scored higher on tests measuring unusual thoughts-experiences and psychoticism. Moreover, the finding accords with findings from the Edinburgh High-Risk Study that schizotypal features predicted schizophrenia [19]. Our construct *paranoid-schizotypal*, consisting of the items "*unresponsive, reserved, paranoid, schizoid and bizarre*", share features with the cluster-A personality disorders of the DSM IV. Even though the finding was not replicated for the 1947 cohort, the result for the 1957 cohort provides some evidence for a relationship between premorbid cluster-A traits and psychosis vulnerability.

Sensitive-frail and easily hurt

Being assessed as *sensitive-frail* or *easily hurt* more than doubled the risk of developing a psychotic disorder, but only in the 1957 simple model. Since the corresponding items to sensitive-frail and easily hurt were not assessed in 1947 we could not test them in the 1947 cohort. The findings accord with the findings in Swedish male army conscripts [26] that interpersonal difficulties reflecting social anxiety (e.g. feeling more sensitive than others) were associated with an increased risk of developing schizophrenia and other psychotic disorders. It also accords with the finding of anxiety in social interactions being associated with schizophrenia vulnerability in the British 1946 birth cohort [20] and Edinburgh High-Risk Study [19].

Tired-distracted

Being assessed as *tired-distracted* more than doubled the risk of developing a psychotic disorder in the 1957 cohort; the predictor could not be tested in the 1947 cohort. *Age* interacted with *tired-distracted* increasing the risk of psychosis 4% per year of increasing age in probands assessed as *tired-distracted*. This accords with the findings in the Copenhagen High-Risk Project that being unconcentrated and preoccupied at age 15 years was associated with an increased risk of developing schizophrenia [34].

The behaviours and reported symptoms analysed were assessed prospectively and in the probands who developed a psychotic disorder often many years before psychosis onset, which may make them more likely to reflect vulnerability to than the prodrome of psychosis, although the question of the analysed behaviours and reported symptoms best being viewed as vulnerability markers, causal or pathoplastic factors or very early signs essentially remains open [18, 21] since knowledge about aetiology is required to disentangle factors with regard to such effects.

Differences between the 1947- and 1957-cohorts

The predictor *nervous-tense* was significant in both the 1947- and the 1957-cohort but otherwise (although some predictors could only be tested in the 1957-cohort) the predictors reaching significance in the cohorts differed—i.e. *blunt-deteriorated* was significant in the 1947-cohort, while *down-semidepressed* and *paranoid-schizotypal* was significant in the 1957-cohort. The different predictor-profiles found could be the result of different types of cases emerging in the follow-ups of the cohorts (i.e. that predictors of different outcomes were actually analysed). For instance, cases could differ in age at onset of psychosis, type of diagnosis with related type of onset, duration and severity of disorder. The 1947-cohort cases developed psychosis at median age 48.0 years (q1 33.0 years—q3 65.0 years) and the 1957-cohort cases at 46.5 years (q1 28.8 years—q3 70.0 years), thus indicating fairly similar age at onset of psychosis distributions. However, the major part of the 1957-cohort was the healthy survivors in 1957 of the 1947-cohort ($n = 2{,}220$); and these survivors developed psychosis ($n = 26$) at median age 53.5 years (q1 35.0 years—q3 71.2 years), while the new members of the 1957-cohort ($n = 995$, approximately one-third born between 1947 and 1957 and two-thirds immigrated into the Lundby area 1947–1957) developed psychosis ($n = 16$) at median age 36.0 years (q1 22.0 years—q3 56.8 years). Hence, there could be a selection of somewhat more cases with a later onset and less severe disorder in the 1957-cohort as compared to the 1947-cohort. The distributions of diagnoses in the cohorts supports this since the distributions differed between the cohorts in that there was a higher proportion of cases in the 1947- compared to the 1957-cohort who developed schizophrenia (29% compared to 24%) and affective psychosis (33% compared to 26%); and a lower proportion who developed other nonaffective psychoses (i.e. delusional disorder, brief psychotic disorder and psychotic disorder NOS) (16% compared to 26%). It may be that the outcome group of the 1947-cohort was affected by more pervasive psychotic disorders than the outcome group of the 1957-cohort and that this accounts for the different predictor profiles found. It would also be consistent with *blunt-deteriorated* and *paranoid-schizotypal* reaching significance in the 1947- and 1957-cohorts, respectively; *blunt-deteriorated* representing perhaps a sign of more pervasive impending disorder than *paranoid-schizotypal*. Furthermore, the differences between the cohorts may be due to different distributions of predictors.

Specificity of the predictors?—separate analysis of schizophrenia

Our intention was to study behaviour- and personality-related predictors of psychosis broadly since we hypothesized that the early behavioural signs and personality traits that may predict psychosis are unspecific and overlapping in relation to specific diagnostic categories. However, with the finding of different predictor-profiles in the 1947- and 1957-cohorts, perhaps due to different diagnostic distributions in the cohorts, we also studied schizophrenia separately. This was done also to enable a more direct comparison with previous prospective studies on personality-related background factors and psychosis, since most previous studies have studied schizophrenia or schizophrenia spectrum disorders (Table 1). Hereby we found that *abnormal-antisocial* was significant in both the simple and multivariate model for schizophrenia in the 1947-cohort, which may indicate that *abnormal-antisocial* is more closely associated with schizophrenia than with other psychoses [29]. On the other hand, abnormal-antisocial bordered to significance in the simple model for nonaffective and/or affective psychosis in the 1947 cohort; and further: nervous-tense was significant for both schizophrenia (in simple and multivariate models of the 1957 cohort), and nonaffective and/or affective psychosis (in simple and multivariate models of both cohorts), and blunt-deteriorated—which was significant in both simple and multivariate models of the broad psychosis outcome in the 1947 cohort—was almost significant in the simple model for schizophrenia in the 1947 cohort. Taken together, this may be in accord with our hypothesis that predictors of psychosis are unspecific and overlapping between diagnoses, although the small number of outcome events in the models for schizophrenia (1947 cohort $n = 14$, 1957 cohort $n = 11$) limits the possibility for interpretation. Nevertheless, several of the studies in Table 1 found predictors of schizophrenia/schizophrenia spectrum that share some of the features of our predictors; *abnormal-antisocial* (2, 3, 9, 10, 30, 33, 36) and *nervous-tense* (19, 20, 26, 40), respectively. Taken together, the most parsimonious interpretation of our findings at this point may be to view the predictors as predictors of psychosis broadly

Strengths and limitations

The strengths of our study include the following:

(1) that the sample was an unselected, well-defined homogenous community cohort;
(2) the longitudinal design of the study with prospective assessments of predictors in subjects at risk for psychosis before onset of illness, which excluded recall bias to taint the predictor assessments;
(3) the long duration of the study, which increased the likelihood of observing the probands through their periods of risk for psychosis;
(4) the multiple source and best-estimate method of case ascertainment, which may have increased the sensitivity and specificity of diagnoses;
(5) the low attrition between 1947 and 1972, the period during which the majority of the probands passed their principal periods of risk;
(6) the fact that the predictors associated with subsequent psychosis were assessed approximately 9–13 years before illness onset;
(7) that psychiatrists conducted all interviews and evaluated all material from other sources and were in charge of the diagnostic evaluations;
(8) that all first-onset psychosis cases, irrespective of whether they presented to psychiatric care facilities or not and irrespective of age at onset, were included.

The limitations include the following:

(1) the exclusion of cases with psychosis onset before the intake cut-off dates, mirrored by late ages of psychosis onset among the cases of the study, limits the generalization of the results;
(2) the non-validated and not reliability tested assessments of behaviours and reported symptoms, with risk of low measurement precision; the predictors were constructed concepts based upon many variables not making them feasible to be replicated; the behaviours and reported symptoms were clinical assessments meant to represent personality related factors, however, they are more likely to represent a mixture of proper enduring personality traits and fluctuating affective states;
(3) the retrospective application of DSM IV diagnostic rules to prior data (1947–1972) may have resulted in misclassification;
(4) that we regarded the constructed predictors as constant between the investigations, which may have introduced bias;
(5) in pooling the nonaffective and affective psychoses we created a heterogenous outcome group. We did not consider course criteria, like acute or insidious onset, duration, course-type or social/occupational decline in our analyses; and we included all first-episodes from the whole age-range in the same outcome; this makes the interpretation of the results harder as a larger sample size for psychosis was achieved at the expense of specificity of interpretation;

(6) that the number of outcome events for several of the predictors were few (see Table 5);
(7) that the two cohorts were overlapping and that the outcome groups of the cohorts were partly different.

Conclusions

We found some evidence in an unselected community sample for anxiety-proneness, affective/cognitive blunting, poor concentration, personality cluster-A like traits and interpersonal sensitivity to be associated with general psychosis vulnerability. The result was on the whole consistent with findings from earlier studies, although direct comparisons could not be made due to differences of diagnostics and methods.

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