Pathogenesis of schizophrenia: a psychopathological perspective

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Background Despite interest in early treatment of schizophrenia, premorbid and prodromal symptomatology remain poorly delineated.

Aims To compare pre-illness symptomatology in patients at high risk of schizophrenia who progress to illness with that of high-risk subjects who remain well and with normal controls.

Method Using Present State Examination (PSE) data, symptomatic scales were devised from participants of the Northwick Park Study of first-episode schizophrenia and scores were compared on the first and last PSEs of participants of the Edinburgh High Risk Study.

Results At entry, when still well, high-risk individuals who subsequently became ill (mean time to diagnosis 929 days; s.e.=138 days) scored significantly higher on 'situational anxiety', 'nervous tension', 'depression', 'changed perception' and 'hallucinations' than those remaining well and normal controls, who did not differ. With illness onset, affective symptomatology remained high but essentially stable.

Conclusions In genetically predisposed individuals, affective and perceptual disorders are prominent before any behavioural or subjective change that usually characterises the shift to schizophrenic prodrome or active illness.

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Although the phenomenology of schizophrenia is well delineated, the symptomatic profile prior to diagnosis and the progression to illness have not been characterised reliably.

Background

There are three strands to the literature on pre-illness features associated with schizophrenia. First, it has been well established that in childhood and the years before evidence of schizophrenia emerges, individuals differ from normal controls on a range of measures, including psychological test performance and patterns of behaviour (Baum & Walker, 1995; Jones, 1997). Such findings frequently are regarded as evidence that schizophrenia is a disorder of neurodevelopment that arises early but in some way is compensated until the typical age of clinical onset in young adulthood (Murray & Lewis, 1987; Weinberger, 1987). Second, using retrospective patient and third-party accounts, it has been shown that psychopathology of various kinds can precede the emergence of diagnosable illness by months or years (Chapman, 1966; Hafner *et al*, 1995). Some authors have concluded that the psychotic shift is driven by affective change, either anxiety or depression (Birchwood & Iqbal, 1998; Garety *et al*, 2001), whereas others have concluded that affective change itself is consequent upon disturbances in either cognition or perception (Chapman, 1966), something that would be difficult to determine with even detailed retrospective techniques. Third, greater emphasis has been given recently to minor psychotic or psychotic-like phenomena such as referential ideas, perceptual disturbances and magical thinking, in an attempt to determine the point at which early treatment, especially with antipsychotic drugs, would be appropriate (McGlashan & Johannessen, 1996; McGorry, 1998; McGorry *et al*, 2002; Woods *et al*, 2003).

Although the onset of schizophrenia can be very acute, it is often more gradual and the point at which symptomatology could be regarded as predictive or prodromal, rather than representative of the early features of illness itself, is often far from clear (Beiser *et al*, 1993). Prospective population-based studies utilising the controlled and masked assessment of pre-psychotic states would be impractical, but the possibility of such assessment has arisen within the context of the Edinburgh High Risk Study of schizophrenia.

The purpose of the present study is to relate initial symptomatic assessments of the high-risk participants and controls to those characteristic of patients already ill with a first episode of schizophrenia, with a view to considering whether non-psychotic symptoms are secondary to developing psychosis and to define the characteristics of the pre-illness state in high-risk individuals who eventually progress to an acute schizophrenic illness.

METHOD

The Edinburgh High Risk Study concerns young people at enhanced risk of developing schizophrenia by virtue of having at least two close relatives affected by the illness (Hodges *et al*, 1999; Johnstone *et al*, 2000). Participants aged 16–24 years were recruited and were considered to be well at that point. They have been followed up for 9 years, with the prediction at outset that 10–15% would develop schizophrenia. A total of 162 high-risk individuals were recruited, along with two control groups: well young people without a relevant family history (n=36); and patients with a first episode of schizophrenia but no family history of the disorder (n=37). The size of the control samples was determined by the number of high-risk individuals anticipated to develop schizophrenia.

The first-episode controls were seen only once, at the point of their initial assessment, but the high-risk participants and the well controls were seen every 18 months and assessed in psychopathological, neuropsychological and imaging terms (Johnstone *et al*, 2005).

The instrument chosen for assessing the presence of psychopathology was the 9th edition of the Present State Examination (PSE; Wing *et al*, 1974), conducted at entry and at each follow-up. This had been chosen because of its reliability in providing a standardised diagnosis that would be

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used, along with ICD–10 (World Health Organization, 1993), to classify those high-risk individuals who developed a formal schizophrenic illness and who thereby had reached the end of their participation in the study. The PSE is a very detailed instrument giving a standardised assessment of a wide range of symptomatology and therefore would be helpful in evaluating the extent of any psychopathology shown by the high-risk participants and controls.

When the study was designed, it had been predicted that those destined to develop schizophrenia would show a range of prodromal symptoms, which were likely initially to be non-specific in nature but would be followed by the emergence of referential ideas, magical thinking, etc., as much of the recent literature has suggested. It had been anticipated that those who were not going to develop schizophrenia within the study period would be little different from the normal controls, with both groups showing some non-psychotic symptomatology.

These predictions were not altogether borne out. Clinical symptoms of all kinds occurred in high-risk participants and controls but all were more marked in the high-risk individuals, in whom symptoms increased with the passage of time. Possibly psychotic phenomena such as referential ideation and magical thinking occurred in many more of the high-risk individuals than were ever anticipated to develop schizophrenia and considerable degrees of anxiety and depression were found in the high-risk sample at the outset, long before those individuals had developed psychotic features. The CATEGO diagnostic programme (for the PSE) was not helpful in the assessment of this because it does not give emphasis to non-psychotic symptomatology not scoring as severe.

At the outset, when designing the study, we were conscious of the need to limit the number of assessments in order not to overburden the participants and thereby reduce the likelihood of their persisting in the programme. In retrospect, we regret that no well-established psychopathological rating scale sensitive to change, such as the Positive and Negative Syndrome Scale (PANSS; Kay *et al*, 1987), was included in the design. In view of the findings that the study has produced, it seems important, however, to attempt to unlock some of the trends that the data suggest. Consequently, we sought to develop a rating scale from the PSE using data from a large alternative sample to which we had access. This comprised the admission PSEs of the 229 individuals assessed for the Northwick Park Study of first episodes of schizophrenia (Crow *et al*, 1986; Johnstone *et al*, 1986) who received a diagnosis of schizophrenia. These assessments were conducted within 2 weeks of admission for a first psychotic illness and often were done within the first week, before antipsychotic treatment had been instituted.

From this data-set we derived 12 severity scales rating 'situational anxiety', 'nervous tension', 'depression', 'mania', 'overactivity', 'disorganisation', 'changed perception', 'hallucinations', 'disorder of possession of thought', 'delusional construction', 'outside control' and 'negative symptoms'. The derivation and details of these scales are shown in the Appendix. Comparing the scores derived from patients with an already established first episode of schizophrenia (and hence exhibiting those features inherently part of the acute syndrome) with those of the participants of the Edinburgh High Risk Study at entry and over time, we were able to provide an analysis of baseline phenomena and their evolution, with an attempt to identify those that may be harbingers of illness.

Analysis

The PSE data on participants entering the Edinburgh High Risk Study were available at entry on 175 individuals, divided into 127 high-risk participants who remained well through follow-up, 21 who developed a first formal schizophrenic illness (i.e. high-risk ill participants) and 27 normal controls. One-way analyses of variance (ANOVAs) were run, comparing these three groups and the Northwick Park first-episode patients on all the log-transformed symptom scales. Follow-up planned comparisons, not assuming equal variances, compared the 21 high-risk ill participants with the other Edinburgh High Risk Study groups and also to the Northwick Park patients. Non-parametric Kruskal–Wallis tests also were run and in all cases they confirmed the overall parametric findings. Possible gender effects were examined, using χ^2-tests to assess group composition and two-way ANOVAs to search for interaction effects. A separate comparison was made of the Northwick Park patients with high-risk participants who fell ill and were assessed *at the time of illness onset*. A second analysis examined changes in symptoms between the first and last assessments for the Edinburgh High Risk Study participants. This was attempted using repeated-measure ANOVAs, with group (high-risk ill, high-risk well and control) as a between-participants variable.

RESULTS

Results are shown in Table 1. The first part of the table shows that, at entry, those individuals who subsequently fell ill had higher scores than the normal controls and those high-risk participants who remained well on 'situational anxiety', 'nervous tension', 'depression', 'changed perception' and 'hallucinations'. Furthermore, their scores on 'situational anxiety' were significantly greater than those of the Northwick Park sample. On none of the scales did those destined to become formally ill score significantly less than the controls and those destined to remain well. They did, however, score significantly less than the Northwick Park sample on 'depression', 'overactivity' 'disorganisation', 'changed perception', 'hallucinations', 'disorder of possession of thought', 'delusional construction', 'outside control' and 'negative symptoms'. Those who became ill did not differ significantly from the Northwick Park sample on 'nervous tension' or 'mania'.

In the last two columns of Table 1, high-risk participants who fell ill are compared *at the time of their illness* with the Northwick Park patients. The mean scores of the high-risk group are now similar to those of the Northwick Park patients. Only two significant differences remain: on 'situational anxiety' the high-risk participants' scores are higher and on 'delusional construction' they are lower than the Northwick Park patients.

The groups were similar in gender composition (controls, 40.7% female; high-risk well, 53.5%; high-risk fell ill, 42.9%; Northwick Park, 41.4%; χ^2=5.1, NS). No significant interactions between gender and group were discovered on any of the scales.

Scores were calculated for each group from their entry PSE and the last PSE conducted. Because the high-risk sample was drawn from all over Scotland, formal PSEs were available only at illness onset on 19 of those who became unwell. Results are shown in Fig. 1. As would be anticipated, 'psychotic' symptomatology covered by 'disorganisation', 'hallucinations', 'disorder of possession of thought', 'delusional

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construction' and 'outside control' increased significantly in those who became formally ill, as did 'negative features' (time, group and interaction terms all significant, $P<0.001$), and significant deterioration also was evident in 'changed perception'. No significant changes occurred in the other participant groups, who continued to hold to low and stable symptomatic levels. On the other hand, 'situational anxiety', 'nervous tension' and 'depression' remained high in those who fell ill, significantly more so than in the controls and high-risk participants remaining well.

DISCUSSION

Methodology

The methodology adopted in this study is unusual and the reasons why it was adopted require explanation. At the planning stage, the primary objective of interest lay in establishing 'caseness'/'non-caseness', an aim to which the PSE as traditionally used is eminently suited. It subsequently became clear that symptomatology at entry was more prominent and less group specific than the literature or our own predictions had led us to believe and that it was desirable to make more detailed measurements. In the absence of other measures sensitive to symptom change it was decided to adapt the PSE for this purpose.

The PSE is an extensive instrument comprising 140 elicited and observed mental state phenomena, most of which are recorded as continuous variables along a range of 'absent'/'mild'/'severe', and it proved a relatively straightforward matter to construct the 12 scales with high α coefficients (see below and Appendix). In many ways they are similar to other measures of mental state and would be expected to be reliable, valid, sensitive to change and inclusive. The PANSS now has been incorporated into the study and the new PSE scales will be compared with these ratings at completion.

The 12 scales were derived from one of the largest samples of patients with first-episode schizophrenia to which the PSE was applied on admission (i.e. the Northwick Park sample). These patients were early in the course of their florid illness and for the most part only briefly exposed or not exposed at all to psychotropic medications. Because the PSE applies to the previous 4 weeks, it is unlikely that medication or other factors relating to admission significantly altered the ratings in this sample, which may be taken as generally representative of the illness in its acute state. This

Table 1 Mean symptom scores in participants from the Edinburgh High Risk Study and Northwick Park patients with first-episode schizophrenia

Scale	Control (n=27)	High-risk well (n=127)	High-risk fell ill, assessed at entry (n=21)	Northwick Park patients (n=229)	Overall F	High-risk ill v. high-risk well +controls (t)	High-risk ill v. Northwick Park patients (t)	High-risk ill assessed at illness (n=19)[1]	High-risk ill assessed at illness v. Northwick patients (t)
Situational anxiety (scale range 0–12)	0.30	0.60	1.48	0.32	9.26***	2.61*	3.22**	1.32	2.13*
Nervous tension (range 0–18)	1.15	1.75	3.52	4.08	20.41***	2.25*	1.05 NS	3.84	0.07 NS
Depression (range 0–41)	0.85	1.13	3.81	6.59	75.16***	2.93**	2.82**	5.95	1.11 NS
Mania (range 0–6)	0.26	0.16	0.33	0.35	1.06 NS	–	–	0.32	0.44 NS
Overactivity (range 0–12)	0.00	0.08	0.14	0.67	17.21***	1.08 NS	3.65***	0.53	0.41 NS
Disorganisation (range 0–16)	0.00	0.02	0.19	1.11	41.44***	1.31 NS	5.32***	1.26	0.31 NS
Changed perception (range 0–14)	0.26	0.20	0.71	1.64	25.50***	2.27*	2.23*	1.74	0.76 NS
Hallucinations (range 0–19)	0.04	0.14	0.52	4.51	97.97***	2.47*	8.84***	2.74	1.75 NS
Disorder of possession of thought (range 0–14)	0.00	0.00	0.24	1.67	48.44***	1.71 NS	6.17***	1.63	0.27 NS
Delusional construction (range 0–22)	0.00	0.04	0.67	12.34	539.32***	1.71 NS	15.07***	7.89	2.12*
Outside control (range 0–16)	0.00	0.00	0.19	4.14	131.71***	1.77 NS	13.71***	2.89	0.87 NS
Negative symptoms (range 0–14)	0.00	0.01	0.24	1.01	37.53***	1.30 NS	4.32***	0.58	1.20 NS

1. Present State Examination scores at illness onset were unavailable for two participants.
*$P<0.05$; **$P<0.01$; ***$P<0.001$.

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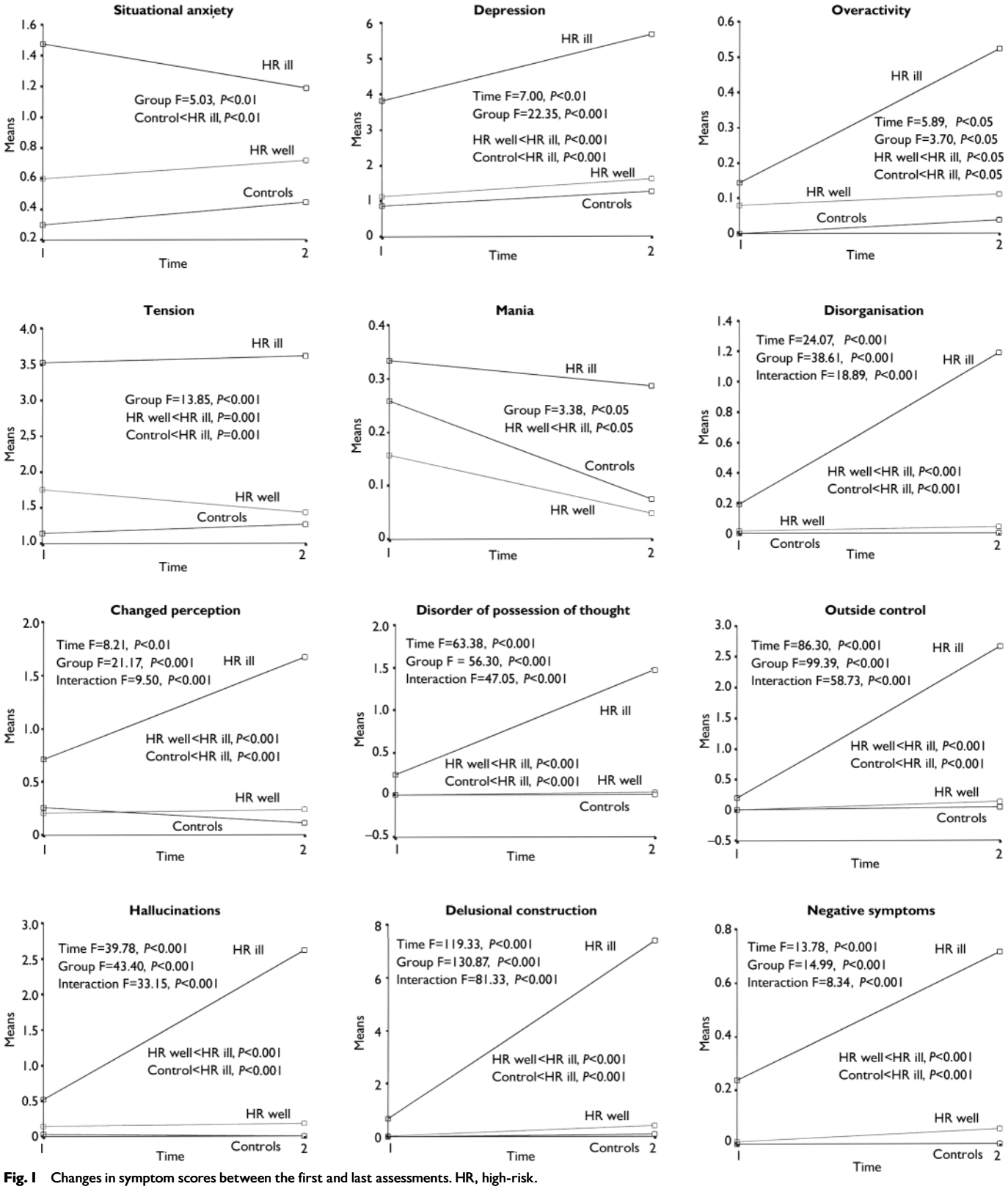

Fig. 1 Changes in symptom scores between the first and last assessments. HR, high-risk.

sample was preferable to the first-episode patients participating in the Edinburgh High Risk Study, in view of its much larger size and the fact that the Edinburgh patients mainly had been exposed to significant antipsychotic drug treatment, sometimes for months, by the time their PSEs were conducted.

The concept of schizophrenia has not changed radically in the 20 years separating the two studies, and the PSE remains a valid instrument. However, different raters were involved in the two studies, raising the question of reliability. Both E.C.J. and D.G.C.O. conducted PSEs in both studies

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and did the great majority in the second phase of the Edinburgh High Risk Study. In addition, for many years they ran a PSE training course, the first such course to be approved outside the Institute of Psychiatry. Research colleagues all received their clinical training in the same institutions as those in which the principal authors worked – a factor known to improve reliability (Kendell, 1975) – and in addition underwent similar PSE training.

Thus, notwithstanding its limitations, we believe that the material presented here is reliable and valid.

Pre-illness symptomatology

This study shows that high levels of non-specific, affective symptoms are evident in patients with first-episode schizophrenia substantially before the onset of psychosis and that these separate those high-risk individuals destined to develop schizophrenia from the other high-risk individuals who remain well. These non-specific abnormalities remain essentially stable over time (and in most instances by 'time' we mean more than 2 years), both in those who progress to illness and in those remaining well, despite a non-significant tendency for 'situational anxiety' to diminish and 'depression' to exacerbate in those who progress to illness. These results suggest that such non-specific affective symptomatology is not merely secondary to emerging psychosis but is more fundamental to the illness process that it antedates. Furthermore, entry scores comprising 'situational anxiety' were significantly higher in those destined to progress to psychosis than in the sample who had been diagnosed with a first episode of schizophrenia (the Northwick Park sample), supporting the view that anxiety-type phenomena may partially remit as psychotic features escalate. Although this study cannot address the question of whether a greater risk accrues from anxiety (Garety *et al*, 2001; Turnbull & Bebbington, 2001) or depression (Birchwood & Iqbal, 1998), a key role for anxiety is in keeping with other results from the Edinburgh High Risk Study, in which the best predictors of illness from mothers' accounts recorded on the Childhood Behaviour Checklist (Achenbach *et al*, 1991) were withdrawn and deviant behaviour, which includes anxiety and depression (Miller *et al*, 2002). Using different measures, participants in the Israeli high-risk study who subsequently progressed to a schizophrenic-spectrum diagnosis were found to have had higher pre-illness levels of anxiety assessed at age 16 years (Kugelmass *et al*, 1995). Thus, anxiety phenomena may be an inherent part of the pathophysiological process mediating the schizophrenic syndrome.

The more specific symptomatology associated with pre-illness states relates to perceptual abnormalities and comprises both distortions and deceptions. Although 'changed perception' and 'hallucinations' were found in normal controls and high-risk participants who remained well, hallucinations in particular were infrequent but were more evident at entry in those who progressed to illness. Abnormalities of thought form and content did not differ significantly between the groups at entry. Group scores were very low and these features were found only in those destined to become ill. Together they comprised the major changes associated with formal illness development.

Premorbid or prodromal?

In the high-risk population, the mean time to illness onset was 929 days (s.e.=138). Because it has been reported that prodromal symptomatology can be present for many years prior to formal diagnosis (Hafner *et al*, 1999), this raises the question of what type of phenomenology the high-risk participants who fell ill were exhibiting at entry – premorbid or prodromal.

Interest in the pre-diagnostic phenomena associated with schizophrenia is long-standing but has increased markedly in recent years. Based on the wish to introduce earlier treatment that may have a favourable impact on outcome, attempts have increased to delineate the prodromal phase of illness from both its premorbid characteristics and the features of the florid first psychotic episode. There is a wealth of evidence that schizophrenia is associated with a wide range of premorbid deviations evident in a series of behavioural, neuropsychological and even brain structural domains – observations confirmed in the Edinburgh High Risk Study sample (Lawrie *et al*, 1999; Cosway *et al*, 2000). These are essentially stable characteristics that do not necessarily result in disadvantage and are certainly not viewed as 'clinical' phenomena. What is less clear is how the illness prodrome (representing the first shift from the premorbid state towards illness) should be conceived: what features it comprises, how it evolves and where its 'break' points lie between normality and illness. This is an increasingly important question because present conceptualisations of prodrome, essentially derived from retrospective methodologies, have led to the advocacy of early treatment interventions with antipsychotic drugs, often in very young individuals. A significant impact on progression to psychosis has yet to be reported extensively (e.g. McGorry *et al*, 2002) and it remains unclear that very early interventions do result in better long-term outcomes.

A major problem is the definition of 'prodrome' in the context of schizophrenia, which of necessity is a retrospective concept (Yung & McGorry, 1996; Cornblatt *et al*, 2001), whose constructs have arisen largely on the basis of interviews with patients already diagnosed and, in more recent work, with their families, supplemented with reference to medical records. Although this methodology may produce systems of assessment that are reliable (Hafner *et al*, 1999), the sources of bias continue to challenge their validity. Using these methods, current views of the contents of the prodrome do include a prominent place for non-specific symptomatology, including affective features, as reported here.

Chapman, on the basis of patient interviews conducted within 3 years of a first episode, found 'intense anxiety' to be 'almost invariable' and also that perceptual disorders were common, something he placed in a key role in his theory on the origins of florid symptomatology (Chapman, 1966). This also would be compatible with our finding that, on entry, those who eventually became unwell demonstrated higher levels of perceptual abnormalities than the other two Edinburgh High Risk Study groups.

Thus, on this evidence, our high-risk sample destined for illness may indeed have been 'prodromal' at entry. However, no matter how the schizophrenic prodrome is conceptualised, some element of change from a previous state (essentially behavioural, but also subjective) is inherent to the concept (Keith & Matthews, 1991; Hafner *et al*, 1992; Loebel *et al*, 1992; Beiser *et al*, 1993; Yung & McGorry, 1996; Cornblatt *et al*, 2001). This key criterion did not apply to the participants of the Edinburgh High Risk Study, who were selected specifically on the basis of being well at entry, in both their own and their families' eyes. Because these individuals came from families in which at least two

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members were already affected with schizophrenia, we take this information, especially that from family sources, as sound.

This might suggest that change need not be an inherent part of the schizophrenic prodrome, which if true would make the concept more arbitrary and difficult to pin down clinically than is currently believed. An alternative proposal might be that high levels of affectivity and perceptual aberration can, in a stable behavioural context, represent part of the premorbid state, perhaps the result of a gradual process of adaptation to underlying cognitive deficits.

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APPENDIX

Derivation of PSE scales

The PSE data from the Northwick Park Study of first episodes of schizophrenia were reduced to those who received CATEGO diagnoses of S+/S?, P+/P? or O+/O?, corresponding to schizophrenic psychoses, paranoid psychoses or 'other' psychoses (Wing *et al*, 1974). The protocols from the resulting 229 patients were used in the derivation of 12 scales.

The PSE is set out in 20 sections: 17 sections comprising symptomatology elicited by formal questioning; and 3 sections for recording mental state features observed during interview. Within these sections most of the items are rated on one of three anchor points, from absent to severe.

The scales were constructed in four stages.

Stage 1

The starting point lay in six broader groupings of the original 20 sections, corresponding to 'anxiety', 'depression', 'manic reaction', 'perceptual disorder', 'delusions' and 'negative symptoms', as follows:

Group 1: *Anxiety* – health; worrying; tension; autonomic anxiety; items 105, 106 ('insight'); item 120 ('behaviour, affect and speech').

Group 2: *Depression* – thinking, concentration, etc.; depressed mood; self and others; item 121 ('behaviour, affect and speech').

Group 3: *Manic Reaction* – expansive mood and ideation; items 111–116, 122, 124, 126, 127, 129 and 135 ('behaviour, affect and speech').

Group 4: *Perceptual Disorder* – derealisation and depersonalisation; other perceptual disorders;

Table A1 Composition of the symptom scales

Scale	Items included	Derivation α (*n*=229)[1]	Confirmatory α (*n*=143)[2]
Situational anxiety	14. Panic attacks		
	15. Situational autonomic anxiety		
	16. Autonomic anxiety on meeting people		
	17. Specific phobias	0.73	0.78
	18. Avoidance of anxiety-provoking situations		
Nervous tension	4. Worrying		
	5. Tension pains		
	6. Tiredness		
	7. Muscular tension		
	8. Restlessness		
	10. Feeling of nervous tension	0.75	0.76
	11. Free-floating autonomic anxiety		
	12. Anxious foreboding with autonomic accompaniments		
	120. Observed anxiety		
Depression	19. Inefficient thinking		
	20. Poor concentration		
	21. Neglect due to brooding		
	22. Loss of interest		
	23. Depressed mood		
	24. Hopelessness		
	25. Suicidal plans or acts		
	27. Morning depression		
	29. Self-depreciation		
	32. Guilty ideas of reference		
	33. Pathological guilt		
	34. Loss of weight due to poor appetite	0.80	0.85
	35. Delayed sleep		
	36. Subjective retardation		
	37. Early waking		
	121. Observed depression		
Mania	41. Expansive mood		
	42. Ideomotor pressure	0.88	0.91
	43. Grandiose ideas		
Over-activity	111. Agitation		
	112. Gross excitement		
	113. Irreverent behaviour		
	122. Histrionic		
	123. Hypomanic affect	0.66	0.80
	127. Lability of mood		
	131. Pressure of speech		
Disorg-anisation	114. Distractibility		
	115. Embarrassing behaviour		
	116. Mannerisms and posturing		
	126. Perplexity		
	129. Incongruity of affect	0.66	0.65
	132. Non-social speech		
	135. Neologisms		
	136. Incoherence of speech		
Changed perception	47. Derealisation		
	48. Depersonalisation		

(*continued overleaf*)

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Table A1 (*continued*)

Scale	Items included	Derivation α (*n*=229)[1]	Confirmatory α (*n*=143)[2]
	50. Heightened perception		
	51. Dulled perception		
	52. Changed perception	0.71	0.41
	53. *Déjà vu*		
Halluci-	60. Non-verbal auditory hallucinations		
nations	62. Voices discussing the patient		
	63. Voices speaking to the patient		
	64. Dissociative hallucinations		
	65. Mind or ears	0.69	0.71
	66. Visual hallucinations		
	68. Olfactory hallucinations		
	70. Other hallucinations		
Disorder of	55. Thought insertion		
possession	56. Thought broadcast		
of thought	57. Thought echo		
	58. Thought block	0.62	0.53
	59. Thoughts being read		
Delusional	72. Delusions of reference		
construc-	73. Delusional misinterpretation		
tion	74. Delusions of persecution		
	80. Physical forces		
	93. Systematisation of delusions	0.79	0.85
	94. Evasiveness		
	95. Preoccupation with delusions and hallucinations		
	96. Acting out delusions		
Outside	71. Delusions of control		
control	75. Delusions of assistance		
	76. Delusions of grandiose abilities		
	78. Religious delusions		
	79. Paranormal phenomena	0.71	0.66
	81. Control by alien forces		
	82. Primary delusions		
	92. Delusions of catastrophe		
Negative	108. Self-neglect		
symptoms	110. Slowness		
	119. Catatonic movements		
	128. Blunted affect	0.65	0.66
	130. Slow speech		
	133. Muteness		
	134. Restricted quantity of speech		
Items not	1, 2, 3, 9, 13, 26, 28, 30, 31, 38, 39, 40, 44–46, 49, 54, 61, 67,		
included	69, 77, 83–91, 97–107, 109, 117, 118, 124, 125, 137–140		

1. Cronbach's α in the derivation sample.
2. Cronbach's α in the confirmatory sample.

thought reading, etc.; hallucinations; item 118 ('behaviour, affect and speech').

Group 5: *Delusion* – delusions.

Group 6: *Negative Schizophrenia* – items 108, 110, 119, 128, 130, 133 and 134 ('behaviour, affect and speech').

Stage 2

In order to determine how many scales could be derived reasonably from these six groups, an initial principal components analysis, using the scree test, was carried out on the items within each group. On the basis of these analyses:

Anxiety was divided into situational anxiety and nervous tension.

Depression remained undivided.

Manic Reaction was divided into mania, overactivity and disorganisation.

Perceptual Disorder was divided into changed perception, hallucinations and disorder of possession of thought.

Delusion was divided into delusional construction and outside control.

Negative Schizophrenia remained undivided.

Stage 3

Cronbach's α coefficients were calculated for each of the 12 scales and adjustments were made to improve these, where possible, by deleting some items, moving others and including a few that had not been included previously.

Stage 4

Cronbach's α coefficients for each of the 12 scales were reassessed in a mixed sample of patients comprising 26 with first-episode schizophrenia in hospitals local to Edinburgh in 1994, 19 high-risk patients who fell ill (assessed at the time of their illness) and 98 patients from Northwick Park with psychoses not classified as schizophrenia.

The details of the final scales derived are set out in Table A1.

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CLINICAL IMPLICATIONS

- In the genetically predisposed, those who develop schizophrenia have prominent affective and perceptual symptomatology before evidence of the change in behaviour or subjective mental state conventionally used to delineate onset of prodromal illness.
- In symptomatic terms, the prodromal phase of illness may be difficult to delineate from the stable premorbid state using retrospective methodologies.
- The prominence of affective phenomenology raises the possibility of early interventions other than antipsychotic drugs.

LIMITATIONS

- The method of data analysis in this study is novel and requires validation.
- The use of data from samples acquired many years apart raises questions of reliability.
- Although data on the high-risk participants were acquired prospectively, the number progressing to a first schizophrenic illness was relatively small.

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