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Premorbid abnormalities in mania, schizomania, acute schizophrenia and chronic schizophrenia

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Abstract The aim of this study was to examine the hypothesis that differences in outcome among affective and non-affective psychoses are associated with differences in the degree of developmental deviance. We conducted a retrospective survey of first contact cases treated over a 20-year period in a psychiatric hospital serving a catchment area in South London. All patients with non-depressive functional psychoses residing in the catchment area who received their first psychiatric treatment between 1965 and 1984 were included in the study. Cases were classified according to the relative chronicity of their illness into four non-overlapping groups: mania, schizomania, acute schizophrenia and chronic schizophrenia. There was a linear trend in the association between illness chronicity and proxy measures of developmental deviance, such as premorbid unemployment, single status and poor academic achievement. Compared to individuals with mania, schizophrenic patients had a 3–6 times increased risk of premorbid abnormality. For patients with schizomania and acute schizophrenia, the risk was 1.5–3 times greater than for manic subjects. We conclude that the prevalence of premorbid abnormalities is highest among chronic schizophrenia, but similar disturbances also occur, to a lesser degree, in less disabling affective and non-affective psychotic disorders.

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Introduction

There is a growing body of evidence that some chronic mental and physical disorders originate during childhood or possibly during foetal development (Kraepelin 1919; Fish 1977; Watt 1978; Barker et al. 1989; Barker and Osmond 1986; Fine et al. 1985). In line with the traditional Kraepelinian distinction between schizophrenia and manic-depressive psychosis, most of the psychiatric research on premorbid abnormalities has focussed exclusively on schizophrenic patients. More recently, however, attention has been drawn to the fact that a substantial proportion of patients with affective disorders have a similar chronic and disabling course as those with schizophrenia (Piccinelli and Willkinson 1994; Clayton 1981). As both in affective disorder and in schizophrenia premorbid abnormalities are associated with poor outcome (Duggan et al. 1990; Stoffelmayr et al. 1983), there is reason to believe that in both disorders a (possibly similar) type of developmental abnormality is associated with a chronic illness course in at least a proportion of cases. Recent studies have investigated neurobiological and neurodevelopmental hypotheses involving non-psychotic disorders, such as affective disorder, neurotic disorder and personality disorder (Dolan 1994; Hollander et al. 1990). Some evidence has emerged suggesting that individuals with affective disorders show subtle differences in cognitive and socio-behavioural development (Done et al. 1994a, b; Rogers 1990), similar to those found in samples of patients with schizophrenia. However, the degree of developmental deviance found in schizophrenia is certainly more conspicuous than that found in affective disorder (Foerster et al. 1991; Jones et al. 1993); similarly, in acute schizophrenia these premorbid abnormalities appear less prevalent than in the severe, early onset forms of the disorder (Foerster et al. 1991; Murray and O'Callaghan 1991). Thus, rather than making absolute distinctions between diagnostic categories, it may be useful to investigate the

hypothesis that the degree of developmental deviance in psychiatric disorders varies as a function of the tendency of a particular disorder towards poor outcome and chronicity. Such a hypothesis would be compatible with the differences in the prevalence of childhood abnormalities between acute and chronic schizophrenia and between schizophrenia and affective disorder. We wished to examine the hypothesis that premorbid abnormalities may be found in both affective and non-affective psychotic disorders, and that risk of developmental deviance would reflect risk of poor outcome and chronicity of the disorder.

Method

Sample

The Camberwell Cumulative Psychiatric Case Register (Wing and Hailey 1972) provides a comprehensive list of all persons from the area of Camberwell in South London who had their first contact with the psychiatric services between 1964 and 1984. With the permission of the Maudsley Hospital ethics committee, a printout was generated from the register of all first-contact patients between 1965 and 1984 who received a non-depressive psychotic register diagnosis: "mania" or "hypomania" (equivalent ICD codes 296.0, 296.2, 296.4), "schizophrenic psychosis" (including schizoaffective type; ICD codes 295.0–295.9), "paraphrenia" (ICD 297.2) or "other non-organic psychosis" (ICD 298.1–298.9). This broad sample was chosen to avoid the possibility of missing any patients who had been inappropriately labelled, and to allow for variation in diagnostic habits. As this was a study of risk, and not rates, no corrections were made for missing data.

Diagnosis

All the case notes of the subjects in this study were traced and scrutinized. Subjects were subsequently given a diagnosis on the basis of operationalized definitions of psychiatric illness.

In a previous study, case notes of patients with an ICD diagnosis of schizophrenia and related conditions (including "schizoaffective disorder", "paraphrenia" and "atypical psychoses") had been scrutinized and rated by D.C. and S.W. (Castle et al. 1991) using the Operational Criteria Checklist for Psychotic Illness (OCCPI) and the OPCRIT computer program, which generate a range of operational definitions for psychotic illness such as the Research Diagnostic Criteria (RDC), DSM-III, DSM-III-R, etc. (McGuffin et al. 1991). Inter-rater reliability, based on 50 cases rated by both D.C. and S.W., was good (kappa = 0.82 for RDC diagnoses). Cases from this sample with an RDC diagnosis of mania or schizomania were also identified.

All the case notes of patients with a register diagnosis of mania or hypomania were also scrutinized and rated with the OCCPI checklist by two of the investigators (N.T. and J.v.O.), but only the OCCPI items necessary to make an RDC diagnosis (Spitzer et al. 1978) were rated. Inter-rater reliability for cases with a register diagnosis of mania was assessed on a random subset of 15 case records, which were rated by N.T. and J.v.O.; kappa for RDC diagnoses was 0.78.

The two authors who rated the manic cases (N.T. and J.v.O.) and one of the authors who rated cases of schizophrenia and related disorders (D.C.) took part in a reliability study of OPCRIT. The mean kappa for the three pairs of raters for RDC diagnoses of schizophrenia and affective psychosis was 0.74 (range: 0.70–0.76).

Diagnostic comparisons

In the comparison between diagnostic categories on premorbid, clinical and demographic variables, four non-overlapping groups of patients were defined. These included: (1) RDC mania; (2) RDC schizomania; (3) "acute" schizophrenia; (4) "chronic" schizophrenia. Chronic schizophrenia was defined as a condition characterized by typical delusions and/or hallucinations (Schneider 1959) and meeting DSM-III-R (APA 1987) criterion B (deterioration from premorbid level of functioning), criterion C (schizoaffective and mood disorder ruled out) and criterion D (continuous signs of disturbance for at least 6 months). Acute schizophrenia indicated a condition with typical delusions and/or hallucinations and DSM-III-R criterion C, but not meeting criterion B and criterion D. The rationale for this division into acute and chronic schizophrenia was to create two schizophrenic syndromes, broadly corresponding to the British notions of acute and chronic schizophrenia (Van Os et al. 1993).

The four diagnostic categories were ordered according to their prognostic implications, based on the well-established evidence (Westermeyer and Harrow 1988; Tsuang and Dempsey 1979) that (1) affective psychoses (i.e. mania and schizomania) have a better outcome than non-affective schizophrenic psychoses (i.e. acute and chronic schizophrenia), and that (2) among the affective psychoses, schizoaffective disorders have a worse prognosis and (3) schizophrenia defined in terms of deterioration from premorbid level of functioning and persistance of symptoms has a worse prognosis than acute schizophrenia without these signs. Thus, the order (from favourable to poor prognosis) was: mania, schizomania, acute schizophrenia, chronic schizophrenia.

Demographic data

Other information systematically obtained for all individuals included: sex, age at first contact, date of birth, and ethnicity and country of birth of both patient and parents. "Ethnicity" categories were white European, Afro-Caribbean, African, Asian and "other", while "country of birth" categories were United Kingdom and Eire, West Indies (Caribbean), Asia, Africa and "other". These data were rated directly from the case records; checks on date of contact, date of birth and country of origin were made from the front sheets of the case notes and the Camberwell Register itself. Checks on ethnicity ratings were made on a subset of 34 patients using data from previous direct-interview studies involving these patients; no erroneous ratings were found. Childhood social class was defined as paternal occupation as recorded in the notes (categorized into "unemployed", "manual work", "white collar" and "professional"). In a previous study (Castle et al. 1993) paternal occupation data from 20 randomly selected case records of the same sample were compared with information recorded on birth certificates, which routinely record such information. Despite a few minor dissimilarities (e.g. exact description of job), no errors were found.

Patients who were living outside the catchment area at the time of first contact but had erroneously been included in the register were excluded. Similarly, checks were made on first-contact status to preclude bias due to inclusion of "false" first-contact cases (see above).

The following variables were used as indicators of premorbid social and academic development: academic achievement (no examinations, CSE, O level, A level and tertiary education); premorbid employment ("unemployed" = 6 or more months of unemployment in the previous 3 years; "unstable" = three or more jobs in the years prior to first contact; "stable" = one job in the years prior to first contact; "not on job market"); marital status (married or living as married). Because of the small number of subjects in some diagnostic groups, premorbid variables were dichotomized ("unemployed", "no examinations", "single") in the analyses.

Table 1 Associations between diagnostic category and measures of premorbid adjustment (*OR* odds ratio)

Measures of premorbid adjustment		Diagnostic category				
		Mania	Schizomania versus mania	Acute schizophrenia versus mania	Chronic schizophrenia versus mania	Test for trend (test statistic)[d]
Premorbid unemployment: unemployed	OR	1[b]	2.8 (0.6–12.7)[a]	2.7 (0.97–8.8)	4.5 (1.8–13.5)	$P < 0.001$ (13.3)
	adjusted OR[c]	1[b]	2.7 (0.7–10.4)	2.3 (0.9–6.3)	5.6 (2.2–13.9)	$P < 0.001$ (18.6)
Academic achievement: no examinations	OR	1[b]	1.1 (0.4–3.5)	1.2 (0.6–2.4)	3.0 1.6–5.8)	$P < 0.001$ (15.4)
	adjusted OR[c]	1[b]	1.8 (0.5–7.1)	1.2 (0.5–2.8)	3.2 (1.4–7.3)	$P < 0.01$ (9.5)
Marital status: single/not cohabiting	OR	1[b]	0.7 (0.3–2.1)	1.1 (0.6–2.2)	1.3 (0.7–2.3)	$P = 0.3$ (1.3)
	adjusted OR[c]	1[b]	0.8 (0.3–2.7)	2.1 (0.9–5.1)	3.0 (1.3–6.8)	$P < 0.05$ (6.7)

[a]95% confidence intervals in parenthesis
[b]Baseline
[c]Adjusted for sex, age of onset, ethnicity and paternal social class (except premorbid employment)
[d]Crude OR, maximum likelihood estimate; Adjusted OR, likelihood ratio statistic

Analyses

The main analyses used odds ratios to estimate the association between diagnostic category and other variables, calculated with the program EGRET (version 0.26.6, Statistics and Epidemiology Research Corporation, North Carolina, USA). All odds ratios refer to mania versus other diagnostic categories. Crude odds ratios, 95% confidence intervals and the test for trend for crude odds ratios were first computed. Odds ratios were adjusted with the logistic regression procedure; confidence intervals and tests for trend for adjusted odds ratios were calculated from the results of the logistic regression.

Results

Sample

Out of 545 patients (88% of a total selection of 621), 71 had an RDC diagnosis of mania (males: 53%) and 24, of RDC schizomania (males: 33%). Ninety-seven patients met our criteria for acute schizophrenia (males: 50%) and 195 subjects met the criteria for chronic schizophrenia (males: 55%). The mean age of onset in males was 35.2 years for mania, 27.6 years for schizomania (compared to mania: $P = 0.2$), 34.5 years for acute schizophrenia (compared to mania $P = 0.8$) and 33.2 years for chronic schizophrenia ($P = 0.5$). In females, the mean age of onset was 33.3 years for mania, 35.6 years for schizomania ($P = 0.6$), 36.3 years for acute schizophrenia ($P = 0.5$) and 50.4 years for chronic schizophrenia ($P < 0.001$). Data on sex, ethnicity and age at first contact with psychiatric services were available for all subjects, data on premorbid employment for 96%, on premorbid academic achievement for 93% and on marital status for 95%.

Premorbid variables

We compared academic achievement, premorbid employment and marital status between individuals with mania and with other diagnoses (Table 1), controlling for gender, age of onset and ethnicity. Because of the possible effect of social class background on education and age at marriage, paternal social class was also controlled for in the comparisons with academic achievement and marital status as the dependent variable. Compared to mania, the odds of being unemployed, single or having left school without examinations tended to increase with illness chronicity, although the trend was not monotonic or similar in magnitude for all measures. The risk of premorbid abnormality in individuals with chronic schizophrenia was 3–6 times greater than for patients with mania, whereas for schizomanic and acute schizophrenic patients the increase in risk was 1.5–3 times. For marital status, differences between mania and chronic schizophrenia only became apparent after controlling for confounders. This was mainly due to the effect of age of onset in females: females with schizophrenia had a much later age of onset, and for that reason were more likely to be married at onset of illness, thus obscuring the difference between manic and schizophrenic individuals.

Employment and education variables are also subject to a cohort effect. Such an effect could have affected subjects with mania and schizophrenia differentially, as there was an excess of older schizophrenic females in our sample who may not have had the same educational opportunities. When year of birth was incorporated into the analysis, in order to test for a possible cohort effect, odds ratios differed only by a trivial amount, and the pattern of results remained the same.

Discussion

In a comparison between mania and other psychotic diagnoses ordered according to prognostic significance (illness chronicity), we found that there was a linear

trend in the association between illness chronicity on the one hand, and premorbid adjustment on the other. Schizophrenia defined in terms of deterioration and persistent psychopathology stood out especially; compared to mania, the odds of having poor premorbid functioning was between 3.0 and 5.6 times higher. However, could these findings be due to bias or confounding?

Methodological issues

A number of methodological issues have been discussed above. Elsewhere, we have discussed possible artefacts such as diagnostic bias, changing referral patterns, misclassification of first-contact cases and missing case notes, demonstrating that these are unlikely to have influenced our results significantly (Castle et al. 1991). This was a study of first-contact cases, ascertained irrespective of age, from a defined area, applying operationalized criteria to comprehensive case-note material. Thus, the sample can be expected to be representative of all schizophrenic and manic patients in Camberwell, avoiding conclusions being drawn about a group that has already been partly selected, especially with regard to age of onset, many studies not including late-onset cases. Although it is possible that mild cases of mania would not have come to psychiatric attention, this, if anything, would have reduced the reported associations as the more severe cases can be expected to show more evidence of developmental deviance. Changes in diagnostic practice will not have affected our results, as all cases were rediagnosed using contemporary operationalized criteria, and we assessed the widest feasible range of diagnoses on the register.

The retrospective nature of our study is a limitation. Premorbid social and occupational functioning is difficult to ascertain reliably from case records. However, we used relatively simple data such as academic achievement, employment and marital status to reduce error. We acknowledge that this approach led to a certain degree of over-simplification of the multifaceted aspects of premorbid behaviour; only cases with the severest forms of premorbid abnormalities will have been detected. The premorbid variables used are probably dependent on factors such as ethnicity, gender and social class, as well as age of onset of illness, but we were able to control for all of these in the analyses. It is likely that academic achievement, employment and marital status are proxies of the same latent variable, premorbid adjustment, and results for all three concurred, thus enhancing the validity of our findings. Despite the relatively large sample of cases, the incidence of a disorder such as schizo-affective mania and the prevalence of paternal unemployment were rare enough to jeopardize the statistical stability in some instances; as a consequence, confidence intervals for estimates were sometimes very wide.

Interpretation of findings

The three different measures of premorbid adjustment we used discriminated, after controlling for social class, between relative severity of psychotic illness, the odds of having poorer premorbid adjustment rising progressively with illness severity. This is consistent with reports of subtle abnormalities, including cognitive changes (Aylward et al. 1984), and abnormal personality traits in childhood and adolescence (Walker and Lewine 1990), especially in patients with more severe forms of schizophrenia (Foerster et al. 1991). However, the increase in the odds ratios from mania to chronic schizophrenia was not monotonic in all measures, and much – but not all – of the trend was accounted for by the high values of the odds ratios in the chronic schizophrenic category. The conservative interpretation, therefore, is that, compared to other diagnostic categories, a severe, possibly "neurodevelopmental" type of chronic schizophrenia is especially, but not uniquely, associated with developmental deviance. Similar premorbid abnormalities may be encountered in other psychotic syndromes, with a higher risk of a schizophrenia-like chronic illness course being associated with an increased likelihood of developmental deviance.

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