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Schizophrenia Research 20 (1996) 105–115

SCHIZOPHRENIA
RESEARCH

Further exploration of a latent class typology of schizophrenia

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Received 1 October 1993; accepted 13 October 1995

Abstract

We previously derived a typology of schizophrenia from a latent class analysis of 447 first-contact non-affective functional psychotic patients from a defined catchment area. Here, using the same sample, we show that the three subtypes, 'neurodevelopmental' (Type A), 'paranoid' (Type B) and 'schizoaffective' (Type C) have different premorbid, phenomenological and treatment response characteristics. A canonical variate analysis of the three subtypes achieved partial separation between the first two subtypes, but the 'schizoaffective' type was less distinct.

Keywords: Schizophrenia; Subtypes

1. Introduction

The clinically heterogeneous nature of schizophrenia was acknowledged in the early descriptions of the disorder by Kraepelin (1893) and Bleuler (1911). While Kraepelin attempted to unify descriptions of individual syndromes by Morel (1860 'démence précoce'), Hecker (1871 'hebephrenie'), and Kahlbaum (1874 'katatonie'), under the umbrella term dementia praecox, Bleuler acknowledged the disorder's clinical heterogeneity, entitling his textbook published in 1911 *Dementia Praecox or the Group of Schizophrenias*. Since then, despite the subsequent emergence of schizophrenia as a single diagnostic entity, the classical Kraepelinian subtypes (hebephrenic or disorgan-

ised, paranoid, catatonic, and simple) have been maintained in most official classifications of psychiatric disorders (e.g., World Health Organization, 1978; American Psychiatric Association, 1987). Whether these classical phenotypic subtypes reflect underlying etiological heterogeneity remains unclear (McGlashan and Fenton, 1991).

Since the etiology of schizophrenia is unknown, indirect methods of validation need to be employed to establish the core syndrome and its subtypes. Robins and Guze (1970) suggested five phases in the establishment of indirect validity, namely: clinical description, laboratory investigation (e.g., searching for biological markers), exclusion of other disorders, follow-up and family studies. Subsequent studies have employed some of these methods to evaluate different definitions of schizophrenia and its subtypes (e.g., Kendell et al., 1979; Murray and Murphy, 1979; McGuffin et al., 1984). These studies have shown considerable variability

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between definitions for different validators, but in general criteria for schizophrenia that include longitudinal variables fare better than those which rely on cross-sectional items of psychopathology (McGuffin et al., 1984; Farmer et al., 1987).

Detailed information published by Kallmann (1938) on a large sample of families of schizophrenics made it possible to examine Kraepelinian subtype concordance among parent–offspring pairs. There was a modest tendency for like to go with like, and reassessment of the data by Slater (1947) showed highly significant concordance for subtype. Despite this ‘family study’ support for classical Kraepelinian subtypes, there have also been many dissenting voices. Clinical subtypes are seldom stable over time (Bleuler, 1978; Tsuang et al., 1980) and Carpenter and Stephens (1979) argued that fluctuations in psychopathological features can occur week by week. Catatonic schizophrenia has also declined dramatically in frequency since the turn of the century (Gelenberg, 1979; Mahendra, 1981), and it has been impossible to demonstrate the characteristic symptom pattern, premorbid features, and age of onset of simple schizophrenia (Stone et al., 1968). In addition, Munoz et al. (1972) have argued that simple and hebephrenic subtypes merely represent cross-sectional descriptions of different degrees of severity rather than stable clinical entities. In light of these problems many authors have attempted to redefine schizophrenia subtypes.

Modern attempts at subtyping schizophrenia have focused respectively on paranoid symptoms (Tsuang and Winokur, 1974), affective symptoms (Tsuang and Simpson, 1984), negative symptoms (Crow, 1980; Andreasen, 1985), course of illness (Strauss and Docherty, 1979), response to treatment (Csernansky et al., 1985), and family history (Murray et al., 1985). Such studies attempt to classify patients according to a single operationalised concept; they are therefore ‘concept-driven’ and ‘univariate’, in that each presupposes a single ‘key’ concept. An alternative approach is to use multivariate statistical techniques to derive subtypes. We call this approach ‘multivariate’ and ‘data-driven’. Important examples of earlier work using this approach include that of Lorr et al. (1963), who identified six psychotic subtypes, and

Carpenter et al. (1976), who used cluster analytic techniques to define four subtypes of schizophrenia (‘usual’, ‘flagrant’, ‘insightful’ and ‘hypochondriacal’). More recent is the study of Farmer et al. (1983), in which cluster analysis was applied to a sample of chronic schizophrenic patients, and two fairly consistent clusters were obtained.

These two approaches are not entirely distinct, since concepts are shaped by previous data, and the choice of variables for multivariate analysis is influenced by the preconceptions of the investigators (Grayson, 1987). We prefer multivariate over univariate approaches to classification, since the latter is simply a degenerate case of the former. Indeed, in an overview of a series of articles on subtyping, Bellack and Strauss (1979) stated that “Even though the concept of subgroups has a considerable history, and even though evidence for such subgroups has been increasingly suggested... the research strategy used in studying the schizophrenia syndrome is still uniformly that of looking for one factor in a relatively small sample. This tendency may be the main reason that no more satisfactory answers have been found to the riddle of schizophrenia.”

Recently, we applied latent class analysis to a catchment area psychiatric register sample of 447 non-affective functional psychotic patients (Castle et al., 1994). The analysis was motivated by the increasing recognition that gender differences are important in the etiology of schizophrenia (Castle and Murray, 1991); specifically, that males are particularly prone to a ‘neurodevelopmental’ form of schizophrenia. Subjects were drawn from the Camberwell Register First-Contact Sample, which has been described fully elsewhere (Castle et al., 1991). The Register recorded all patients from the defined catchment area of Camberwell, in South London, who had first contact with the psychiatric services between the years 1965 and 1984. The sample comprised 91% of all patients on the Camberwell Register, who on their first contact with the psychiatric services had received a Register diagnosis of ‘schizophrenia’ (ICD-9 codes 295.0-.9), ‘schizoaffective disorder’ (ICD 295.7), ‘paraphrenia’ (ICD 297.2), or ‘other non-organic psychosis’ (ICD 298.1-.9). Thus, we selected all patients with a functional psychotic illness which

was not primarily affective. The residual 9% of patients were those for whom case-records were unobtainable. The variables for the analysis were (see Castle et al., 1994, for rationale): (1) family history of schizophrenia in first or second degree relatives (FH); (2) restricted affect (RA); (3) persecutory delusions (PD); (4) poor premorbid social adjustment (SA); (5) dysphoria (DS); (6) early onset, i.e. 25 years or younger (EO); (7) winter birth, i.e. December to April (WB); and (8) male sex (MS). The variables are defined in OPCRIT (McGuffin et al., 1991).

The results from the latent class analysis suggested the existence of three subtypes, which were called 'neurodevelopmental' (Type A), 'paranoid' (Type B), and 'schizoaffective' (Type C). The 'neurodevelopmental' subtype was characterized by early onset (<25 years), poor premorbid social adjustment, restricted affect and male preponderance. In contrast, the 'paranoid' subtype was characterized by later onset, persecutory delusions, and an equal sex ratio, while the 'schizoaffective' subtype was characterized by dysphoria and persecutory delusions, and a female preponderance. In the current analysis, we attempt to characterize the subtypes further using data from the same sample, including variables which were not used in deriving the typology.

2. Method

2.1. Assignment of subjects into subtypes

The patients were the same as those used in the derivation of the latent class typology described above (Castle et al., 1994). Each subject was assigned to one of the classes in the latent class model which we favored (Castle et al., 1994). In this model, each latent class was characterised by a latent class probability and the conditional probabilities of the eight manifest variables. Thus, each subject had a 'prior' probability (the latent class probability) of belonging to a latent class. Then, given his/her values of the eight manifest variables, the 'posterior' probability of his/her belonging to a latent class could be calculated according to Bayes' Theorem and assuming conditional inde-

pendence of the manifest variables. Using, for illustration, the case of three manifest variables, the probability of belonging to latent class x given that the manifest variables have values i , j and k is given by:

$$P(X=x|A=i, B=j, C=k) = \frac{\pi_x \pi_{i|x} \pi_{j|x} \pi_{k|x}}{\sum_{m=1}^L \pi_m \pi_{i|m} \pi_{j|m} \pi_{k|m}}$$

A subject is assigned to the latent class to which he/she has the largest posterior probability of belonging. In this study, the assignment of subjects into latent classes was performed by MLLSA (Clogg, 1977). Once each subject has been assigned to a latent class (and hence a subtype), comparisons between the subtypes can be performed to reveal possible differences.

2.2. Variables

The eight variables which were used in deriving the subtypes were considered separately. The remaining variables were classified into (a) 'premorbid', (b) 'phenomenological', and (c) 'treatment response' characteristics. All variables were dichotomous, being scored 1 if the characteristic was present and 0 if absent. The 'premorbid' variables were:

Family history (other): psychiatric disorder other than schizophrenia in first or second degree relative severe enough to warrant psychiatric referral.

Alcoholism in parents: if either parent was considered (by rater judgement) to have problem drinking or alcohol dependence.

Obstetric complications: rated according to the composite scale of Lewis et al. (1989); this scale has been used previously to rate Maudsley case records (see Lewis and Murray, 1987).

Developmental problems: rated according to the scale devised by Foerster et al. (1991), adapted for use with case records; the scale covers speech, motor and reading difficulties, and enuresis/encopresis. A single composite 'developmental score' was obtained.

Premorbid personality disorder: rated broadly, as in OPCRIT (McGuffin et al., 1991); most patients rated positively for this item showed fea-

tures of paranoid, schizoid and/or schizotypal personality disorder.

Single marital status: subject had never married or lived as married.

Poor premorbid work adjustment: as in OPCRIT; allowance is made for standard of housework, to minimise gender bias.

Unemployment: at illness-onset; full-time students and those engaged in housework fulltime were rated as employed.

Convictions: any convictions up to and including time at first contact; as recorded by the Criminal Records Office and the hospital case records (see Wessely et al., 1993).

Prodromal phase: of at least 6 months as in DSMIII-R (American Psychiatric Association, 1987).

To reduce the number of variables concerned with 'phenomenology', items in OPCRIT (McGuffin et al., 1991) were grouped as follows:

Depressive symptomatology: any one of slowed activity, agitated activity, loss of energy/tiredness, loss of pleasure, poor concentration, excessive self-reproach, suicidal ideation, initial insomnia, early morning wakening, excessive sleep, loss of appetite, loss of weight, increase in appetite and increase in weight.

Manic symptomatology: any one of excessive activity, reckless activity, pressured speech, increased self-esteem, thoughts racing, distractibility, reduced need for sleep, elevated mood and irritable mood.

Unspecified affective symptomatology: affective symptoms predominated or schizophrenic symptoms occurred at the same time as affective symptoms (rater judgement).

Schneiderian first rank symptoms: any one of thought insertion, thought withdrawal, thought broadcast, thought echo, third person auditory hallucinations, running commentary, delusional perception and delusions of passivity.

Thought disorder: if speech was difficult to understand or incoherent, or if positive formal thought disorder was present.

Negative symptomatology: any one of paucity of thought or speech, blunted affect, or rapport difficulty.

Paranoid delusion: any one of well-organised

delusions, grandiose delusions, delusions of influence, and wide-spread delusions.

Non-Schneiderian auditory hallucinations: any one of persecutory/jealous hallucinations, abusive/accusatory/persecutory voices and other (non-affective) auditory hallucinations.

Inappropriate affect: as described in OPCRIT.

Bizarre delusions: as in OPCRIT.

Bizarre behaviour: as in OPCRIT.

Catatonia: as in OPCRIT.

The only variable on 'treatment response' was:

(1) Response to neuroleptics: if schizophrenic symptoms responded to neuroleptics (rater judgement), as in OPCRIT.

Ratings on all items were performed before the latent class typology was derived.

2.3. Analysis

If the proposed typology has validity, then the subtypes should differ from each other in a range of characteristics, including those not used in the derivation of the subtypes. Thus, we examined the frequency distributions of the above binary variables in the three subtypes, and tested the differences between subtypes using the chi-squared test of homogeneity.

To further characterize the differences between the three subtypes, we performed a canonical variate analysis with the above variables. Canonical variate analysis (sometimes called canonical discriminant function analysis) attempts to highlight group differences from multivariate data by the formation of a small number of composite variables which show maximal variation between groups but minimal variation within groups (Marcia et al., 1979; Krzanowski, 1988). The first canonical variate, also called the first canonical discriminant function, is defined as the linear combination of variables with the maximum ratio of between-group to within-group variances, subject to a normalization constraint. The r th canonical variate is defined as the linear combination of variables with the maximum ratio of between-group to within-group variances, again subject to a normalization constraint but also to it being uncorrelated with the first $r-1$ canonical variates. The maximum number of canonical vari-

ates is one less the number of groups, or one less the number of variables, whichever is smaller. Canonical variate analysis is widely used as a method of data exploration and display, rather than formal hypothesis testing. For this purpose, it can be used with both continuous or, as in this study, binary data.

We used the DSCRIMINANT command of SPSS-PC for the canonical variate analysis. In view of the very large number of variables, we selected a stepwise procedure with the WILKS method, so that at each step the variable which maximized Wilks' lambda (Marcia et al., 1979) was included until no variable met the inclusion criterion. First, the default criterion for inclusion (partial $F > 1.0$) was used, then the analysis was repeated using a more stringent criterion, namely $p < 0.05$.

3. Results

The characteristics of the three subtypes in terms of all the above variables are given in the tables. As expected, large differences are apparent in the variables originally used in the latent class analysis to derive the subtypes (Table 1). No p values are given for these differences, because it is not reasonable to test for group differences in characteristics used to define the groups. More remarkable are the differences in variables not used in the latent class analysis. Thus, among 'premorbid' variables (Table 2a), Type A is characterised by a relatively high frequency of obstetric complications, develop-

mental problems, premorbid personality disorder, single marital status, poor premorbid work adjustment, positive conviction history, and long prodromal phase. Indeed, all positive 'premorbid' features were commoner in Type A than in Types B or C, with the exception of family history of psychiatric disorder other than schizophrenia, which was commonest in Type C.

In terms of the 'phenomenological' variables (Table 2b), the subtypes did not differ significantly in first rank symptoms, auditory hallucinations or bizarre delusions. This is not surprising as patients required such symptoms to be included in the sample. Type A had the highest frequencies of thought disorder, negative symptoms, manic symptomatology, inappropriate affect, bizarre behaviour and catatonia. The high rate of 'manic' symptoms may reflect the broad definition used; for example, 'distractibility' could also be a sign of acute schizophrenic psychosis. Type B had the highest frequency of paranoid delusions. Type C had the highest frequencies of depressive symptomatology and unspecified affective symptoms. Differences in response to neuroleptic treatment (Table 2c) were only marginally significant, with Type A being the least and Type C the most frequently responsive.

When $F > 1$ was used as the inclusion criterion, 23 variables were entered into the canonical variates. The first canonical variate, with an eigenvalue of 4.42, had large positive loadings (> 0.2) from early onset, poor premorbid social adjustment, restricted affect, dysphoria and male sex, and large negative loadings (< -0.2) from persecutory delu-

Table 1
Comparing the subtypes in terms of variables used in the latent class analysis

Characteristic	Percentage present		
	Type A ($N=168$)	Type B ($N=175$)	Type C ($N=83$)
Family history schizophrenia	10.7	8.8	0.0
Restricted affect	23.0	3.8	0.0
Persecutory delusions	57.9	87.9	95.4
Poor premorbid social adjust	61.8	21.4	18.4
Dysphoria	50.6	19.8	100.0
Onset <25 years	85.4	1.6	12.6
Winter birth	38.8	52.7	35.6
Male sex	69.1	57.1	0.0

Table 2

Comparing the subtypes in terms of (a) 'premorbid', (b) 'phenomenological', and (c) 'treatment response' variables

Characteristic	Percentage present			p value
	Type A	Type B	Type C	
(a) Premorbid				
Family history of other psychiatric disorders	32.0	20.9	36.8	0.0100
Alcoholism in parents	11.8	9.3	3.4	0.0863
Obstetric complications	14.9	3.4	2.4	0.0042
Developmental problems	11.0	5.9	2.1	0.1007
Premorbid personality disorder	31.5	8.8	9.2	<0.0001
Single marital status	86.5	39.6	33.3	<0.0001
Poor premorbid work adjustment	61.2	25.4	29.9	<0.0001
Unemployed	66.3	59.1	51.7	0.0656
Convictions	42.6	22.6	12.9	<0.0001
Prodromal phase	62.4	50.8	44.8	0.0130
(b) Phenomenological				
Depressive symptomatology	64.0	40.7	86.2	<0.0001
Manic symptomatology	39.3	25.3	31.0	0.0165
Unspecified affective symptoms	34.3	17.6	54.0	<0.0001
First rank symptoms	57.3	53.8	52.9	0.7268
Thought disorder	37.6	25.3	12.6	0.0001
Negative symptoms	51.1	29.1	21.8	<0.0001
Paranoid delusions	73.6	89.6	85.1	0.0003
Auditory hallucinations	62.9	69.8	75.9	0.0883
Inappropriate affect	21.3	8.8	13.8	0.0034
Bizarre delusions	25.3	21.4	17.2	0.3194
Bizarre behaviour	53.4	36.8	51.7	0.0037
Catatonia	10.7	3.8	1.1	0.0025
(c) Treatment response				
Response to neuroleptic	71.3	77.5	85.1	0.0435

sions and winter birth. The second canonical variate, with an eigenvalue of 1.16, had large positive loadings from male sex, manic symptomatology and winter birth, and large negative loadings from dysphoria, response to neuroleptics and persecutory delusions (Table 3a). The first canonical variate therefore appears to be a contrast between the features of an early, severe illness and those of a predominantly paranoid condition. A large negative score on the second canonical variate, on the other hand, is associated with the presence of dysphoria, good response to neuroleptics, and being female. Plotting the data on the two canonical variates (Fig. 1) shows three fairly distinct clusters corresponding to the three subtypes.

Using the more stringent inclusion criterion of $p < 0.05$, only 11 variables were entered into the canonical variate. The pattern of loading (Table 3b) is similar to the less stringent analysis,

so that the previous interpretations apply. However, the plot of the data on the canonical variate (Fig. 2) now shows only two fairly distinct clusters, with Type C not well separated from Type B.

4. Discussion

The current study has several limitations. Our data were obtained retrospectively from hospital case records, rather than directly from the patients. Although the quality of the case records was generally high, certain items, particularly those concerning the distant past, or distant relatives, may not have been accurately recorded. Moreover, items in OPCRIT are dichotomous, so that some information on severity is lost. However, while the data may lack precision, they are at least unbiased,

Table 3
The coefficients of canonical variate, inclusion criteria (a) $F > 1$
and (b) $p < 0.05$

Variable (in order of inclusion)	1st canonical variate	2nd canonical variate
(a) $F > 1$		
Early onset	0.9891	-0.1208
Dysphoria	0.2477	-0.7815
Male sex	0.2336	0.6036
Poor premorbid social adjustment	0.2975	0.0956
Persecutory delusions	-0.3151	-0.20641
Restricted affect	0.2851	0.1618
Winter birth	-0.2196	0.2428
Response to neuroleptic	0.0445	-0.3348
Manic symptomatology	0.1562	0.2919
First rank symptoms	0.1434	0.1196
Paranoid delusions	-0.1837	0.1519
Bizarre delusions	0.1349	0.0329
Inappropriate affect	-0.0885	-0.1175
Alcoholism in parents	0.1346	0.1128
Single marital status	0.1143	0.0724
Bizarre behaviour	0.0522	-0.1700
Developmental problems	-0.1274	0.0584
Obstetric complications	0.1061	0.0651
Unemployed	-0.0955	0.1556
Poor work adjustment	0.0143	-0.1955
Unspecified affective symptoms	-0.0888	-0.1401
Catatonia	-0.1246	0.0453
Family history of other psychiatric disorders	0.0788	-0.1173
(b) $p < 0.05$		
Early onset	0.9749	-0.1406
Dysphoria	0.2437	-0.8346
Male sex	0.2359	0.6382
Poor premorbid social adjustment	0.3400	0.1218
Persecutory delusions	-0.2955	-0.1998
Restricted affect	0.2916	0.1542
Winter birth	0.1913	0.2721
Response to neuroleptics	0.0285	-0.3816
Manic symptomatology	0.0820	0.2161
First rank symptoms	0.1885	0.1254
Paranoid delusions	-0.1416	0.1813

since ratings were made before the latent class analysis, and without knowledge of the proposed typology. Random measurement errors are more likely to reduce statistical power than to lead to false positive results.

To the extent that the three subtypes differ from each other in a wide range of variables, these

results do support the validity of the latent class typology. Thus, broadly defined schizophrenia may be a mixture of two, and possibly three, syndromes. There is an early onset, severe form (Type A) which affects men more frequently than women. This form is associated with premorbid social maladjustment, personality disorder and positive conviction history, and has a high frequency of restricted and inappropriate affect, negative features, thought disorder, and catatonia. It should be pointed out that not all these variables are independent of each other; for example, poor premorbid work adjustment would be expected to correlate strongly with poor premorbid social adjustment, which is one of the variables used in the original definition of the latent class typology (Castle et al., 1994). Having said this, a number of other variables also showed highest prevalence in Type A, namely of a family history of schizophrenia and of a history of obstetric complications, factors which have been implicated in the etiology of the neurodevelopmental abnormality in schizophrenia (Lewis and Murray, 1987; Jones and Murray, 1991; Murray et al., 1992). Obstetric complications have been reported to be particularly associated with male and early onset schizophrenia (O'Callaghan et al., 1992).

The second fairly distinct subtype (Type B) usually manifests at a later age and is a milder illness with prominent paranoid delusions but much less restricted affect, negative features and thought disorder. A family history of schizophrenia is slightly less common in this type than in the more severe form, but is nevertheless substantially above the rate expected in the general population. Interestingly, 52% of the patients in this subtype had a date of birth between December and April. This is consistent with several studies which have found a greater winter birth excess among schizophrenic patients with a less chronic course of illness. For example, Dalen (1975) identified a winter/spring birth excess only in patients hospitalised less than 2 months, while Pulver et al. (1983) found a January/February/March birth excess only in patients hospitalised less than 6 months (see Bradbury and Miller (1985) for a full review). Nasrallah and McCalley-Whitters (1984) found that a greater number of paranoid males

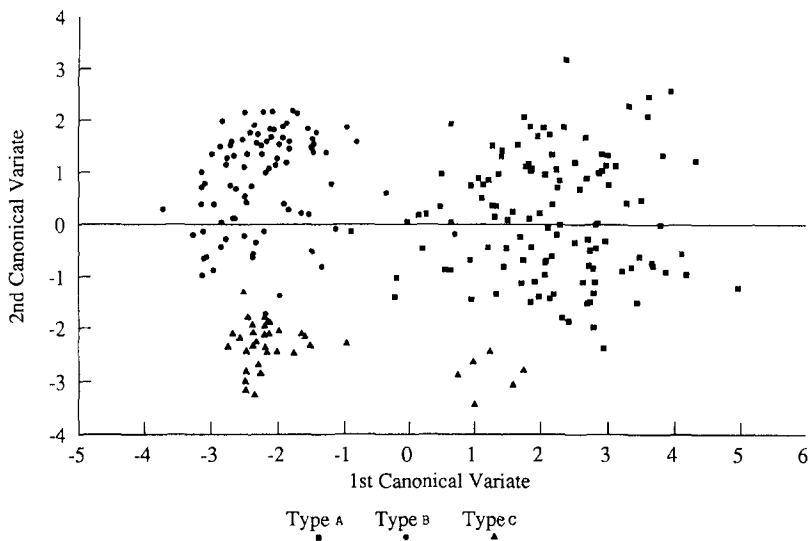


Fig. 1. Plot of data on first two canonical variates (inclusion criterion $F > 1$).

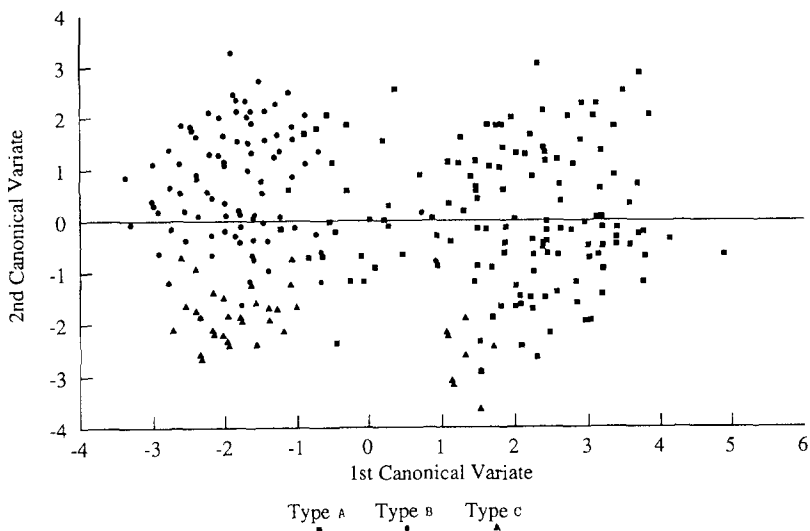


Fig. 2. Plot of data on first two canonical variates (inclusion criterion $p < 0.05$).

and non-paranoid females were born during winter months, but Hsieh et al. (1987) found an excess of winter births only among paranoid males, and Torrey et al. (1977) found no subtype difference in season of birth.

To the extent that Types A and B are similar to the classical hebephrenic and paranoid subtypes

of schizophrenia, our results are supportive of the classical subtypology, without the catatonic and simple forms. Our results are therefore similar to those of Tsuang and Winokur (1974), who classified a group of schizophrenic patients into hebephrenic and paranoid subtypes by clinical judgment, and found that hebephrenics had earlier

onset, more flat affect and thought disorder, higher familial morbidity, and worse outcome. Similarly, Farmer et al. (1983) performed a hierarchical cluster analysis, and found two reasonably distinct clusters, an H type characterised by family history of schizophrenia, poor premorbid adjustment, early onset, bizarre behaviour, blunted affect, and incoherent speech, and a P type with well organised delusions. Interestingly, although Kraepelin regarded some cases of paranoid psychosis as variants of dementia praecox, he also commented on the difficulties of defining the boundaries of the disorder: “The most criticism has always been directed against the inclusion of the paranoid forms in dementia praecox... how wide the circle of paranoid cases must be drawn, which we are justified in regarding as expressions of that disease” (Kraepelin, 1919). In part, Kraepelin’s argument for a single disease entity was based on his inability to find a clear separation between subtypes: “Everywhere the same basic disturbances recur again and again... not all of these characteristics can be demonstrated in each and every case. Nevertheless the survey of a large number of complete observations teaches us that we never find a picture which does not show a link by very gradual transitions with all the others...” (Kraepelin, 1909).

The canonical variate analysis achieved a partial separation between Types A and B. This raises the possibility that they are distinct disorders. Indeed, most patients classified as paranoid or hebephrenic either remain so, or become undifferentiated over time; changes from one subtype to the other are rare (Kendler et al., 1985; Parnas et al., 1988; Fenton and McGlashan, 1991). However, Farmer et al. (1984) found that the rates of both H and P subtypes were significantly higher in the cotwins of H type probands when compared to cotwins of P type probands. They therefore suggested that the two subtypes were not genetically distinct, but were more likely to represent varieties of the same disorder that occupy “different positions on the same multifactorial continuum of liability”. In support of this view, a lower genetic loading in paranoid schizophrenia, compared to non-paranoid schizophrenia, has been reported in many previous studies (reviewed by Kendler and Davis,

1981); although a subsequent study by Kendler et al. (1988) found no such difference. Moreover, studies on subtype concordance in multiply affected families have yielded conflicting results (Kendler and Adler, 1984; McGuffin et al., 1984; Jorgensen et al., 1987; Kendler et al., 1988). The data in the current study do not allow us to examine the genetic overlap between Types A and B. However, we have demonstrated a wide range of differences between the two types, as well as a partial separation using the canonical variate analysis. It is possible, therefore, that there are some unique etiological factors for these two subtypes.

In addition to Types A and B, our sample also contains a group of patients with prominent dysphoria (Type C). These patients often had a family history of psychiatric disorders other than schizophrenia (mostly affective disorder), which suggests aetiological differences from the other two subtypes. In a comparison of DSM-III schizophrenic patients with and without a family history of affective disorder, Kendler and Hays (1983) found that those patients with a family history of depression were more likely to develop a depressive syndrome during follow-up. However, since the results of the canonical variate analysis did not clearly separate out Type C from the other subtypes, it is not clear whether dysphoric patients constitute a group distinct from the first two subtypes.

Further work is necessary to replicate this typology in a separate sample, and to develop improved operational criteria for the subtypes. In addition, further studies on subtype concordance in twins will clarify the extent of genetic overlap of the subtypes. Whether the subtypes have correlates with brain morphology can be studied by modern neuroimaging techniques.

Acknowledgment

This work was supported in part by a Wellcome training fellowship in mental health (Pak Sham) and in epidemiology (Simon Wessely), and an MRC training fellowship in epidemiology (David Castle).

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