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The underlying structure of diagnostic systems of schizophrenia: A comprehensive polydiagnostic approach

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Abstract

The objective was to ascertain the underlying factor structure of alternative definitions of schizophrenia, and to examine the distribution of schizophrenia-related variables against the resulting factor solution. Twenty-three diagnostic schemes of schizophrenia were applied to 660 patients presenting with psychotic symptoms regardless of the specific diagnosis of psychotic disorder. Factor analysis of the 23 diagnostic schemes yielded three interpretable factors explaining 58% of the variance, the first factor (general schizophrenia factor) accounting for most of the variance (36%). On the basis of the general schizophrenia factor score, the sample was divided in quintile groups representing 5 levels of schizophrenia definition (absent, doubtful, very broad, broad and narrow) and the distribution of a number of schizophrenia-related variables was examined across the groups. This grouping procedure was used for examining the comparative validity of alternative levels of categorically defined schizophrenia and an ordinal (i.e. dimensional) definition. Overall, schizophrenia-related variables displayed a dose-response relationship with level of schizophrenia definition. Logistic regression analyses revealed that the dimensional definition explained more variance in the schizophrenia-related variables than the alternative levels for defining schizophrenia categorically. These results are consistent with a unitary and dimensional construct of schizophrenia with no clear "points of rarity" at its boundaries, thus supporting the continuum hypothesis of the psychotic illness.

Keywords: Psychosis; Schizophrenia; Diagnosis; Classification; Diagnostic criteria

1. Introduction

Diagnosing schizophrenia has been problematic since the earliest clinical descriptions of the disorder, and the existence of basic disagreements in the concept is reflective of the large number of competing diagnostic systems that have been proposed over the last hundred years. The magnitude of the problem is well illustrated by the finding that diagnostic systems may vary as many as sevenfold in their rates of diagnosing schizophrenia (Endicott et al., 1982). Furthermore, diagnostic systems of schizophrenia have been criticized on the basis of their unestablished construct validity and arbitrariness (Fenton et

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al., 1981). These problems have been interpreted by some authors as the demonstration of the existence of something profoundly wrong in the schizophrenia concept (Brockington, 1992).

Diagnostic schemes of schizophrenia, including those claiming to be based solely on descriptive or pragmatic considerations, are actually rooted in a number of assumptions that according to Berner et al. (1992) are: (a) schizophrenia is a discrete category; (b) Kraepelin's outcome principle involving that schizophrenia leads to deterioration; (c) Bleuler's pathogenic basic disturbance that states that some symptoms (i.e. thought disorganization) are the expression of a putative primary brain disturbance; (d) Jaspers's hierarchical principle stating that certain symptoms (i.e. 'schizophrenic' symptoms) do have diagnostic prominence over others (i.e. mood symptoms); and (e) Schneider's psychological principle stating that bizarre delusions or hallucinations are disorder-specific. Divergences in diagnostic schemes of schizophrenia mostly depend upon the degree to which they take the aforementioned principles into consideration, the great variation in diagnostic systems (and therefore in their defining features) being a direct expression of this. Beyond these theoretical considerations, other two putative factors could also explain variability among definitions, namely, the existence of different disorders within the schizophrenia construct, and the dimensional nature of the construct that makes it hardly amenable to be operationalized in terms of categorical definitions. In the first case, the different schizophrenia schemes (or clusters of them) would be the expression of the existence of several underlying discrete disorders, and, in the later case, the different schizophrenia schemes would be, at least in part, the expression of setting different cutoff points to a dimensional construct. All these caveats are directly related to the questions about the boundaries between schizophrenia and other psychotic disorders, and whether categorical definitions of schizophrenia "carve nature at its joints."

Given that the ultimate goal of any diagnostic system is to provide insights into the nature of the disorder, it is essential to examine the accuracy of the diagnostic construct. Previous work has mainly focused on comparing the predictive validity of alternative definitions regarding a number of external variables (Hawk et al., 1975; Stephens et al., 1982; McGlashan, 1984; Endicott et al., 1986). Less attention, however, has been paid to empirically examine the underlying structure of the different diagnostic systems, and we are aware of only two previous studies addressing this question. Gift et al. (1980) applied 9 schizophrenia definitions to a sample of 272 patients admitted for a first episode of a functional psychiatric illness. They found three underlying factors that were difficult to interpret. Bell et al. (1998) applied 11 schizophrenia definitions to a sample of 479 patients admitted for a first psychotic episode. They found a three-factor solution corresponding to modern operational, Kraepelinian/Bleulerian, and Schneiderian diagnostic systems. A major limitation of these two studies was that they were conducted on first-episode samples by which the low illness duration (in the Bell et al., 1998 study the median duration of psychotic symptoms was 1 month) may have precluded to diagnose many patients of schizophrenia according to the longitudinal diagnostic systems. Another problem inherent to the use of first episode samples derives from the existence of some syndrome instability during a few years following the onset of the psychotic illness (McGorry, 1994). Lastly, an additional limitation of these studies is that they used a relatively small number of schizophrenia definitions.

Given both the lack of concordance between the results of the two previous studies and the above mentioned methodological limitations, the underlying structure of the varied schizophrenia definitions remains to be established. The aim of this study was twofold. First, to examine the factor structure of 23 alternative definitions of schizophrenia in a sample of patients with any psychosis very broadly defined, and second, to examine the pattern of associations between the underlying dimensionality and schizophrenia-related variables. We reasoned that the type and number of the factors, together with the study of the distributional properties of the schizophrenia-related variables against the resulting factor structure, may shed light on the nature of the schizophrenia concept itself.

2. Materials and methods

2.1. Subjects

Six-hundred and sixty psychotic patients drawn from consecutive admissions to the psychiatric unit

of the Virgen del Camino Hospital between the years 1988 and 1996 made the study sample. To be included in the study patients had to present at least one psychotic symptom as defined by the DSM-III-R criterion A for schizophrenia or severe negative symptoms. According to this recruitment procedure all patients with psychotic symptoms regardless of the specific type of functional psychotic disorder were eligible for inclusion in the study. Exclusion criteria were severe drug abuse confounding diagnosis, demonstrable brain disease or mental retardation. The study was approved by the local ethical committee, and all subjects or their legal representatives provided written informed consent to participate in the study.

The study group included 384 male (58%) and 276 female (42%) patients having an average education of 9.3 years (SD=3.2). The mean age at index admission was 36.0 years (SD=14.0), the mean age at onset was 26.9 years (SD=10.6), and the average number of hospitalizations was 3.4 (SD=4.3).

2.2. Diagnostic assessment

For the present study the main assessment instrument was the Manual for the Assessment of Schizophrenia (MAS) (Landmark, 1982). This is a semi-structured interview for assessing psychotic symptoms and diagnoses from a polydiagnostic point of view, which was originally designed to cover 12 diagnostic criteria of schizophrenia and related disorders. The schedule was subsequently modified by our group (Peralta and Cuesta, 1992) to rate 11 additional criteria of schizophrenia, specific psychotic disorders, and the whole spectrum of functional psychotic disorders according to DSM-III-R criteria. Given that DSM-IV and ICD-10 diagnostic systems were not available when the study began, and that the expanded MAS contains the necessary information for making diagnosis according to ICD-10 and DSM-IV criteria, the patients were re-diagnosed using these diagnostic systems. A more detailed description of the assessment and diagnostic procedures can be found in Peralta and Cuesta (2003).

The DSM-IV diagnostic breakdown of the study sample was as follow: schizophrenia (n=358, 54.2%), schizophreniform disorder (n=61, 9.2%), schizoaffective disorder (n=37, 5.6%), bipolar disorder (n=64, 9.7%), major depression (n=24, 3.6%), delusional disorder (n=27, 4.1%), brief psychotic disorder (n=57, 8.6%) and psychotic disorder Not Otherwise Specified (NOS) (n=32, 4.8%). Given the relatively low number of patients with major depression, they were subsumed together with bipolar patients under the diagnosis of affective disorder (n=88, 13.3%).

The expanded MAS provides comprehensive information on demographic variables, clinical features, current and past symptoms and signs, and course of the psychotic illness, all of which is used to diagnose each patient according to 23 definitions of schizophrenia, which cover virtually all the meaningful conceptualizations of the disorder from Kraepelin to nowadays. The 23 diagnostic systems and their defining features are presented in Table 1.

To rate the MAS, multiple information sources were used, including several interviews with the patients over the hospitalization period, information provided by relatives, medical records, and nurses' information about the patients' behavior in the ward. Patients were assessed by one of the authors each of them rating approximately half of the patients. Inter-rater reliability for symptoms and diagnoses was assessed by the authors in 33 consecutive patients, which were assessed conjointly but rated separately.

2.3. Procedure and statistics

To examine the underlying structure of the 23 alternative definitions of schizophrenia we have chosen for a categorical principal component analysis, as implemented in the program CATPCA in SPSS categories 10.0 (Norusis, 1999). CATPCA stands for CATegorical Principal Components Analysis with optimal scaling. The technique can be thought of as a method of dimension reduction where no distributional assumptions about the variables are made. It simultaneously quantifies categorical variables while reducing the dimensionality of the data with minimal loss of information found in the original variables. The transformation of the original categorical variables into metric variables is underpinned by monotonically increasing transformation functions. The theory of CATPCA has been extensively described, among others, by Gifi (1991) and Meulman et al. (2002). We also calculated the tetrachoric correlations for the 23 diagnostic systems. This correlation matrix was then factor analyzed and

Table 1
Variables included in 23 alternative diagnostic criteria of schizophrenia

Diagnostic features	Diagnostic system
Inclusion criteria	
Delusions (any)	3, 7, 8, 9, 10, 11, 12, 14, 16, 19, 20, 21, 22
First-rank delusions (any)	1, 6, 16, 17, 21, 22,23
Passivity/control delusions	4, 5, 7, 10, 11, 14, 18, 19, 20
Thought withdrawal	7, 14
Thought broadcasting/reading	8, 14
Thought insertion	14
Primary delusions	4, 5
Bizarre delusions	8, 14, 21, 22
Paranoid delusions	6, 7, 9, 18
Delusions of reference	5, 6, 7
Nihilistic delusions	8
Non-depressive delusions	9
Fragmentary non-systematic delusions	15
Firmly fixed mood–incongruent delusions	18
Hallucinations (any)	5, 6, 9, 10, 12, 14, 19, 21, 22
Auditory hallucinations	4, 18
First-rank hallucinations	14, 16, 17, 21, 22, 23
Non-affective auditory hallucinations	17, 21, 23
Verbal hallucinations	14
Hallucinatory behavior	17
Formal thought disturbances	2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 15, 16, 19, 21, 22
Incoherence	8, 13, 21, 22, 23
Derailment	13, 22
Thought blocking	6, 7, 13, 23
Neologisms	6, 7, 13, 23
Muddled speech	13, 15
Circumstanciality	23
Concreteness	9
Idiosyncratic thinking	9, 15
Bizarre behavior	3, 13, 19
Non-manic, silly, senseless behavior interfering with communication	18
Catatonic symptoms	3, 4, 5, 9, 17, 19, 21, 22, 23
Bizarre mannerisms	6
Stereotypy	7
Negative symptoms	
Affective flattening	2, 3, 4, 5, 6, 7, 8, 16, 20, 21, 22 ,23
Alogia	22, 23
Avolition	5, 22, 23
Social withdrawal	3, 4, 5, 10
Other symptoms	
Ambivalence	2
Autism	2, 5, 9, 10, 11
Praecox feeling	4
Lack of insight	5, 8
Derealization/depersonalization	4, 6, 9
Attentional disturbances	5
Other symptoms	
Poor rapport	8
Inappropriate affect	2, 3, 9, 14, 15, 20, 21, 22
Confusion	9
Deterioration	
No return to the premorbid level of functioning	12, 19
Deterioration	
Definite social deterioration over the period of at least 1 year	19
Social/occupational dysfunction	21, 22
Residual symptoms	
At least 6 months	21
At least 2 years	4, 5, 15
Symptom duration	
2 weeks (psychotic and/or residual symptoms)	14
1 month (psychotic symptoms)	23
6 months (psychotic and/or residual symptoms)	12, 21, 22
Premorbid features	
Schizoid personality	4
Poor premorbid functioning	12
Other clinical features	
Insidious onset	4, 5, 19
Unreliable information	8
Single status	12
Family history of schizophrenia	12
Age at illness onset	
Before 40 years	12, 15
Before 35 years	19
Exclusion or negatively weighted features	
Major affective syndrome (any)	16
Is not a prominent part of the illness	14
Duration brief relative to active and residual periods	21, 22
Does not antedate the schizophrenic symptoms	23
Manic or depressive symptoms	12, 19
Waking early	8
Depressive facies	8
Elation	8
Manic spending sprees	18

Table 1 (*continued*)

Diagnostic features	Diagnostic system
Exclusion or negatively weighted features	
Drug abuse or dependence	
One year before illness onset	12
Two years before illness onset	19
Sensorium disturbances	16
Disorientation	19
Perplexity	19
Family history of affective disorder	19

1 = Schneider, 2 = Eugen Bleuler, 3 = Manfred Bleuler, 4 = Langfeldt, 5 = Kraepelin, 6 = North America, 7 = Great Britain, 8 = Flexible system (cut-off 6), 9 = New Haven Schizophrenia Index, 10 = Yusin, 11 = Newmark, 12 = Feighner, 13 = Vienna Research Criteria, 14 = Research diagnostic Criteria, 15 = Francia, 16 = Taylor and Abrams, 17 = Present State Examination–CATEGO, 18 = Cloninger, 19 = Guze, 20 = Landmark, 21 = Diagnostic and Statistical Manual, 3rd ed. rev, 22 = Diagnostic and Statistical Manual, 4th ed., 23 = International Classification of Diseases, 10th ed.

the results were examined to determine the degree of similarity with the CATPCA results. We used the two classical criteria for selecting the optimal number of factors to retain, namely, eigenvalue >1, and substantive interpretation of the factors.

Given than a general schizophrenia factor accounted for most of the common variance of the factor solution (see below), we wished to examine further whether this factor is compatible either with a categorical or a dimensional concept of schizophrenia within the psychotic population. To do this, the whole sample was divided into n-tiles groups on the basis of the distribution of the general schizophrenia factor score. This approach allows us to derive different levels for defining schizophrenia that can be conceptualized in terms of categories of the disorder defined as specific cutoff points of the n-tiles grouping, or alternatively as an ordinal, and thus dimensional, construct. For example, a quintiles grouping would conceptualize schizophrenia categorically as absent, doubtful, very broad, broad or narrow, and at the same time as a dimensional construct in that the groups are considered as points along a continuum. A similar approach has been used by Kendler and Gardner (1998) to examine the comparative validity of alternative definitions of major depression. By using this approach we aimed at answering the following questions: (i) is there a dose-response association between schizophrenia-related features and levels of schizophrenia definition? (ii) what level of schizophrenia definition best fit the schizophrenia-related features?, and (iii) what type of schizophrenia construct (categorical or dimensional) best fit the schizophrenia-related features?

Schizophrenia-related features were grouped into three sets of variables: main defining symptoms, main defining associated features, and features not included in any schizophrenia definition. Main defining symptoms included lifetime ratings of delusions, hallucinations, first-rank symptoms, formal thought disorder, affective flattening, catatonic symptoms, inappropriate affect, and residual symptoms. Main defining associated features included functional deterioration since the illness onset, six-month duration of symptoms, insidious onset, poor premorbid adjustment, the lifetime presence of a major mood syndrome (mania or depression), and a positive family history for schizophrenia or major mood disorder in the first-degree relatives. The features not included in any schizophrenia definition were selected on the basis of their well-established association with schizophrenia relative to non-schizophrenic psychotic disorders. These included gender male, never married, poor premorbid academic achievement, lack of psychosocial stressors before the index episode, early illness onset (<23 years), poor treatment response at the index episode, and a monomorfous course of the disorder.

The three questions mentioned above were examined using logistic regression analyses. For the first question the OR linear trend statistic was used. For the other two questions, different logistic regression models were built in that the dependent variable was the categorical diagnosis of schizophrenia according to specific n-tile cutoff points and the independent variables were the main defining symptoms, the main associated features, and the features not included in definitions. Furthermore, and to examine the fit of a dimensional schizophrenia construct, an ordinal logistic model was built by entering the n-tile term into the model as the continuous (dependent) variable. The goodness of fit of each logistic regression model (i.e. of each schizophrenia definition) was expressed as the percentage of the variance explained for by the schizophrenia-related variables as reflected by the Cox and Snell pseudo-R^2 statistic. All statistical analysis were done using the SPSS v.10.0 (Norusis, 1999).

3. Results

3.1. Diagnostic systems of schizophrenia

The prevalence and inter-rater reliability for the 23 diagnostic systems is presented in Table 2. The number and percentage of patients diagnosed as schizophrenic by each system varied highly. The most inclusive system (NHSI) diagnosed schizophrenia in 571 patients (86.5%), whereas the most restrictive system (Guze) diagnosed schizophrenia in 190 patients (28.8%). Inter-rater reliability for diagnostic systems was adequate, with no system falling below a κ level of <.40 (fair reliability).

The level of concordance among systems was, in general, very poor, with only 32 out the 253 concordance values falling above a κ level >.50 (substantial concordance). Specific concordance figures for the 23 diagnostic systems are available from the first author on request.

3.2. Principal component analysis

CATPCA for the 23 diagnostic systems resulted in five factors with eigenvalue >1, which explained 68.3% of the variance (Table 2). Three out the five factors had substantive interpretation. The first factor (general schizophrenia factor) was made of most diagnostic systems, with lesser but still substantial loadings for Schneider and Cloninger criteria and low loading for the NHSI criteria. The second factor (Schneiderian factor) had a bipolar structure with positive loadings for criteria including Schneiderian symptoms and negative loadings for criteria indicating chronicity or poor outcome. The third factor (Bleulerian factor) also had a bipolar structure with positive loadings for criteria including loss of associations and negative loadings for RDC, Taylor–Abrams and ICD-10 criteria. The fourth and fifth factors explained a negligible amount of variance accounted for and had no meaningful interpretation.

Table 2
Prevalence, inter-rater reliability, and categorical factor analysis for 23 diagnostic systems of schizophrenia

	Prevalence *N* (%)	Inter-rater reliability κ	Factors				
			I	II	III	IV	V
Schneider	447 (67.7)	.82	.47	.73	−.48	.49	−.32
Eugen Bleuler	318 (48.2)	.64	.82	.12	.64	−.17	−.20
Manfred Bleuler	321 (48.6)	.53	.69	.23	.73	−.32	−.26
Langfeldt	314 (47.6)	.78	.89	−.58	.36	.39	.17
Kraepelin	296 (44.8)	.80	.88	−.54	.32	.42	.15
North America	415 (62.9)	.59	.74	.58	.30	.00	.12
United Kingdom	202 (30.6)	.53	.69	.61	.30	−.01	−.19
IPSS-6	542 (82.1)	.59	.71	.12	−.25	−.32	.06
NHSI	571 (86.5)	.43	.22	.39	−.16	−.42	.99
Yusin	270 (40.9)	.65	.85	.43	.15	.25	−.07
Newmark	497 (75.3)	.57	.71	.42	.17	−.21	.21
Feighner	257 (38.9)	.76	.86	−.52	−.02	.08	.22
Vienna	332 (50.3)	.71	.58	.31	.54	−.67	−.12
RDC	421 (63.8)	.80	.83	.18	−.65	−.30	−.14
France	262 (39.7)	.71	.86	−.43	.44	.20	.31
Taylor–Abrams	459 (69.5)	.64	.80	−.11	−.65	−.44	−.16
PSE	522 (79.1)	.65	.50	.62	−.33	.49	−.25
Cloninger	553 (83.8)	.76	.39	.55	−.44	.14	.47
Guze	190 (28.8)	.61	.74	−.48	−.07	.10	.21
Landmark	205 (31.1)	.73	.61	.58	.09	.51	−.09
DSM-III-R	354 (53.6)	.88	.98	−.47	−.35	−.02	−.12
DSM-IV	358 (54.2)	.88	.96	−.52	−.36	−.03	−.17
ICD-10	419 (63.5)	.83	.91	−.29	−.52	−.23	−.28
Eigenvalue			8.31	2.84	2.21	1.32	1.01
Explained variance			36.15	12.38	9.64	5.77	4.37
Cronbach's alpha			0.92	0.68	0.57	0.26	0.01

IPSS = International Pilot Study of Schizophrenia, NHSI = New Haven Schizophrenia Index, RDC = Research Diagnostic Criteria, PSE = Present State Examination, DSM = Diagnostic and Statistical Manual, ICD = International Classification of Diseases. Factor loadings ≥.50 are underlined.

To examine the effect of chronicity on the factor structure, we split the sample according to the median illness duration (6 years) and performed a CATPCA in the subgroups with an illness duration under (n = 316) and above (n = 344) the median. The same three interpretable factors with only minor differences in factor loadings emerged in each factor analysis. The pairwise Pearson's correlations coefficients for the general schizophrenia, Schneiderian and Bleulerian factors were 0.90, 0.86 and 0.87, respectively.

The factor analysis performed using the tetrachoric correlations matrix resulted in three interpretable factors with eigenvalues greater than 1.0 each of them explaining 56.1%, 17.2%

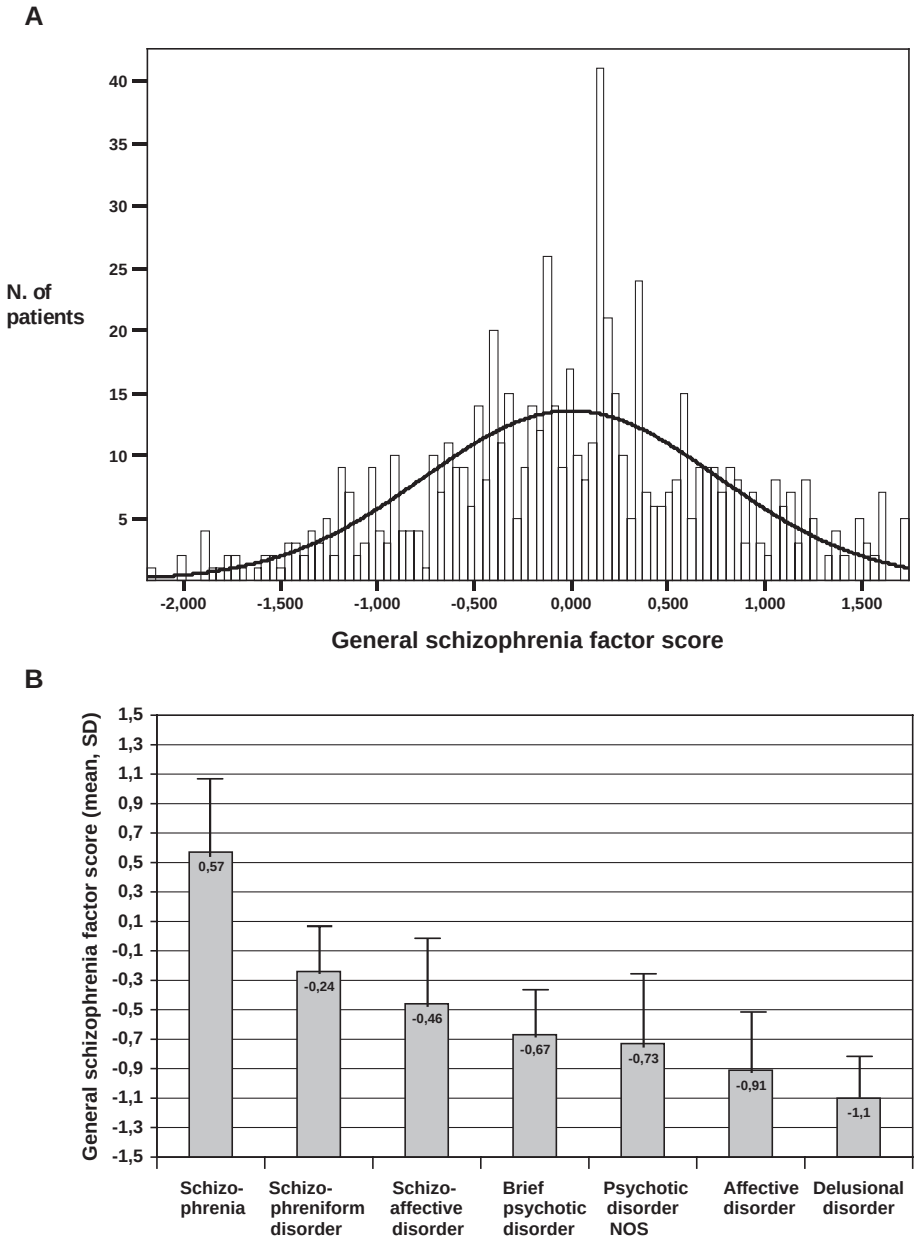

Fig. 1. Distribution of the general schizophrenia factor score in the whole sample (A), and across the DSM-IV classification of psychotic disorders (B).

and 10.5% of the common variance. These three factors were virtually identical in item composition to the first three CATPCA factors as illustrated by the pairwise Pearson's correlations coefficients: 0.83 (general schizophrenia factor), 0.80 (Schneiderian factor), and 0.74 (Bleulerian factor).

Given that the general schizophrenia factor accounted for most of the common variance of the factor solutions both in CATPCA and in factor analysis of tetrachoric correlations, we assumed that this factor best represented the underlying structure of the 23 definitions of schizophrenia. We'll therefore focus on examining the nature of this factor in terms of its distributional properties and relationship with schizophrenia-related variables.

3.3. Distributional properties of the general schizophrenia factor

In order to examine the degree of separation between patients with and without schizophrenia on the basis of the general schizophrenia factor, factor scores were calculated for the 660 patients in the form of standard scores with mean of 0 and standard deviation of 1, and frequency distributions were examined on these scores. Fig. 1A and B, respectively, displays the distribution of the general schizophrenia factor scores in the whole sample of psychotic patients and across the DSM-IV classification of psychotic disorders. Distribution of scores in the whole sample showed a roughly normal distribution, and scores across DSM-IV classification showed a rather continuum distribution from schizophrenia (higher scores) to delusional disorder (lower scores). Neither of these distributional patterns showed any good evidence for a clear separation between schizophrenic and non-schizophrenic patients.

3.4. Distribution of schizophrenia-related variables across levels of schizophrenia definition

We examined three to seven n-tiles divisions of the whole sample on the basis of the general schizophrenia factor scores.

Table 3
Distribution of schizophrenia-related variables by level of schizophrenia definition

	Level definition for schizophrenia					OR linear trend
	Absent No. (%)	Doubtful No. (%)	Very broad No. (%)	Broad No. (%)	Narrow No. (%)	
Main defining symptoms						
Delusions	116 (87.9)	121 (91.7)	123 (93.2)	131 (99.2)	132 (100)	2.04 (1.50–2.79)
Hallucinations	69 (52.3)	105 (79.5)	98 (74.2)	110 (83.3)	122 (92.4)	1.65 (1.43–1.90)
First-rank delusions or hallucinations	43 (32.6)	92 (69.7)	95 (72.0)	96 (72.7)	121 (91.7)	1.85 (1.61–2.11)
Formal thought disturbances	63 (47.7)	72 (54.5)	75 (56.8)	80 (60.6)	114 (86.4)	1.44 (1.28–1.61)
Affective flattening	44 (33.3)	56 (42.4)	85 (64.4)	117 (88.6)	128 (97.0)	2.59 (2.21–3.03)
Catatonic symptoms	24 (18.2)	30 (22.7)	37 (28.0)	31 (23.5)	38 (28.8)	1.12 (0.99–1.28)
Inappropriate affect	28 (21.2)	56 (42.4)	74 (56.1)	104 (78.8)	126 (95.5)	2.56 (2.20–2.98)
Residual symptoms	13 (9.8)	31 (23.5)	60 (45.5)	113 (85.6)	130 (98.5)	4.20 (3.43–5.14)
Main defining associated features						
Functional deterioration	21 (15.9)	29 (22.0)	66 (50.0)	105 (79.5)	130 (98.5)	3.43 (2.87–4.10)
Six-month duration	65 (49.2)	69 (52.3)	91 (68.9)	117 (88.6)	127 (96.2)	2.08 (1.79–2.41)
Insidious onset	23 (17.4)	30 (22.7)	33 (25.0)	56 (42.4)	56 (42.4)	1.41 (1.24–1.59)
Poor premorbid adjustment	19 (14.4)	16 (12.1)	38 (28.8)	41 (31.1)	54 (40.9)	1.48 (1.30–1.70)
Mania	53 (40.2)	39 (29.5)	19 (14.4)	8 (6.1)	5 (3.8)	0.47 (0.40–0.56)
Depression	69 (52.3)	43 (32.6)	32 (24.2)	16 (12.1)	7 (5.3)	0.50 (0.42–0.58)
FH+ for schizophrenia	13 (9.8)	16 (12.1)	14 (10.6)	21 (15.9)	18 (13.6)	1.11 (0.94–1.30)
FH+ for major mood disorder	23 (17.4)	21 (15.9)	15 (11.4)	9 (6.8)	6 (4.5)	0.69 (0.57–0.83)
Features not included in definitions						
Gender (male)	62 (47.0)	72 (54.5)	79 (59.8)	88 (66.7)	83 (62.9)	1.20 (1.07–1.34)
Never married	64 (48.5)	91 (68.9)	104 (78.8)	105 (79.5)	120 (90.9)	1.69 (1.48–1.95)
Poor academic achievement	24 (18.2)	39 (29.5)	51 (38.6)	53 (40.2)	59 (44.7)	1.33 (1.18–1.50)
Lack of psychosocial stressors	64 (49.2)	74 (56.1)	84 (63.6)	91 (68.9)	89 (67.4)	1.19 (1.10–1.28)
Early illness onset	36 (27.3)	65 (49.2)	64 (48.5)	67 (50.8)	90 (68.2)	1.41 (1.26–1.58)
Poor treatment response	20 (15.2)	21 (15.9)	41 (31.1)	57 (43.2)	60 (45.5)	1.55 (1.36–1.76)
Monomorfous course	44 (33.3)	58 (43.9)	82 (62.1)	102 (77.3)	104 (78.8)	1.74 (1.54–1.98)

FH = Family history.

These alternative divisions produced a very similar pattern of results in that the prevalence of most schizophrenia-related variables increased in a monotonic fashion with level of schizophrenia definition. Here only the distributional pattern of schizophrenia-related variables across the quintiles grouping is presented (Table 3). The quintile groups (each composed of 132 patients) would roughly correspond with the following levels of schizophrenia definition: "no" schizophrenia (first quintile), "doubtful" schizophrenia (second quintile), "very broad" schizophrenia (third quintile), "broad" schizophrenia (fourth quintile), and "narrow" schizophrenia (fifth quintile). The number (and percent) of patients with DSM-IV schizophrenia across the quintile groups was, respectively, 1 (0.8%), 29 (22%), 74 (56.1%), 122 (92.4%) and 132 (100%). Thus is, all the patients in the highest quintile group had DSM-IV schizophrenia and only one patient in the lowest quintile group had DSM-IV schizophrenia.

As can be seen in Table 3, most of the variables displayed a dose-response relationship with level of schizophrenia definition. The only variables not showing such an association were catatonic symptoms among the main defining symptoms, and family history for schizophrenia among the main associated features. All the variables not included in definitions showed a dose-response relationship with level of schizophrenia definition. Given that the OR linear trend is no formal test of continuity, we also tested for deviation from linearity as calculated by the chi-square test for linearity. The obtained results remained basically the same as with the OR linear trend, excepting that hallucinations ($\chi^2=14.5$, $df=3$, $p<0.01$), formal thought disorder ($\chi^2=10.3$, $df=3$, $p<0.05$), residual symptoms ($\chi^2=9.5$, $df=3$, $p<0.05$), and first-rank symptoms ($\chi^2=25.8$, $df=3$, $p<0.001$) showed a departure from linearity.

Duration of illness is a potentially confounding variable given both that diagnostic systems highly vary according to duration criteria, and that some schizophrenic features (i.e. functional deterioration, residual symptoms) may take several years to establish. Accordingly, analyses were repeated incorporating duration of illness as covariate. The pattern of results remained unchanged, for example, the adjusted OR for the linear trend between delusions and level of schizophrenia definition was 2.06 (95% confidence interval = 1.52 – 2.80).

3.5. Model fit for the alternative definitions of schizophrenia based on the general schizophrenia factor score

Fig. 2 shows the logistic regression model fit for the categorical definitions of schizophrenia at the level of "doubtful" ($n=528$), "very broad" ($n=396$), "broad"

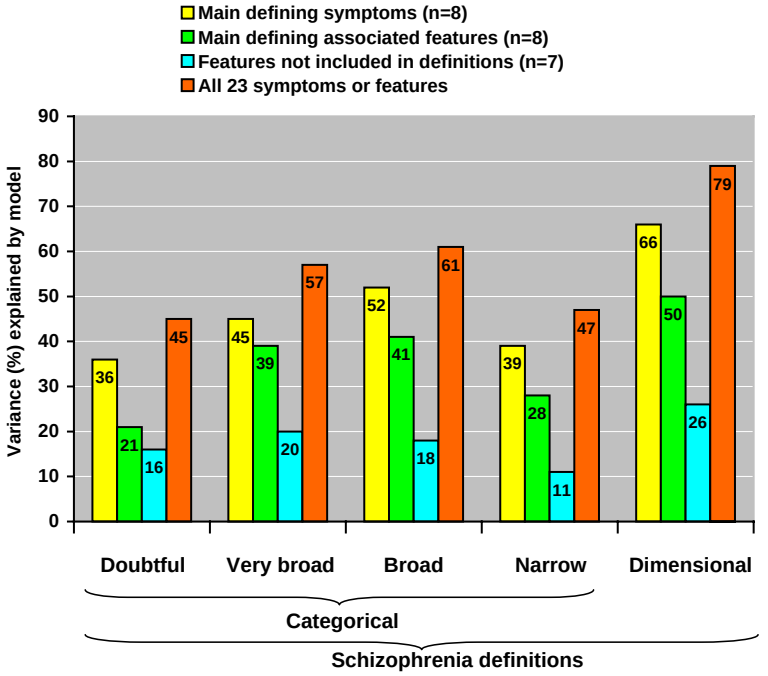

Fig. 2. Logistic regression model fit for four alternative levels of categorically defined schizophrenia and a dimensional definition regarding 23 schizophrenia-related variables.

($n=264$), and "narrow" ($n=132$), as well as for the dimensional definition (from the level of "no" schizophrenia to the level of "narrow" schizophrenia). A consistent pattern of results emerged in that the dimensional construct outperformed the alternative categorical constructs in terms of amount of explained variance in each set of schizophrenia-related variables. Among the categorical models and regarding all the 23 schizophrenia-related variables, the definition at the level of "broad" had the best fit (pseudo-$R^2=0.61$) and the definition at the level of "doubtful" had the worst fit (pseudo-$R^2=0.45$). Overall, schizophrenia definitions at the level of "very broad" or "broad" performed better than the definitions at the level of "doubtful" or "narrow". Again, the pattern of results remained unchanged after adjustment for duration of illness.

4. Discussion

4.1. Main findings

The major findings of this study were as follows: (i) a single unitary construct that we have named general schizophrenia factor underlie most of the diagnostic systems of schizophrenia, (ii) the general schizophrenia factor has a normal distribution within a psychotic population, (iii) the unitary schizophrenia construct seems to be better represented by dimensional than by categorical ordering of typical schizophrenia-related variables, and (iv) among the different levels of categorical definitions of schizophrenia, those defining a relatively broad phenotype appears to have higher validity that those representing narrow or too broad definitions.

The factor structure of schizophrenia definitions obtained in this study is difficult to compare with that obtained in the two previous studies, mainly because differences in illness duration, sample composition and number and type of diagnostic schemes analyzed. The major finding of our study, namely the existence of a general schizophrenia factor, was not found in the previous studies, and deserves to be replicated by other authors. This finding, however, seems to be rather robust in that it was based on a large sample of psychotic patients, a broad coverage of schizophrenia definitions, and it was confirmed across different factor analytical procedures and levels of chronicity.

While the overall poor concordance among diagnostic systems is reflective of the lack of a uniform diagnostic concept of schizophrenia across definitions, the finding of a general schizophrenia factor clearly indicates that systems share a single underlying construct, likewise Spearman's "g" intellective factor best represents different mental abilities (Spearman, 1904). The finding of a general schizophrenia factor is not surprising at all given that the majority of schizophrenia definitions share symptoms such as delusions, formal thought disturbances, hallucinations or some type of negative symptoms (see Table 1). Accordingly, the alternative diagnostic systems seem to represent different aspects of the same construct rather than antagonistic concepts. In fact, Young et al. (1982) using latent class analysis could demonstrate that schizophrenia diagnoses according to RDC, flexible-6, Schneider, and Taylor–Abrams criteria all identified a single underlying diagnostic construct, this despite the relatively low agreement among systems.

In congruence with the normal distribution pattern of the general schizophrenia factor, the distributional properties of schizophrenia-related features across different levels of schizophrenia definition based on this factor clearly showed a dose-response pattern, and no 'point of rarity' was evident at any level of schizophrenia definition. The lack of a dose-response association for catatonic symptoms and family history of schizophrenia with levels of schizophrenia definition is not surprising at all given that catatonic symptoms have been found to be more prevalent in non-schizophrenic psychotic disorders than in schizophrenia itself (Peralta and Cuesta, 2001), and that most psychotic disorders are genetically related to schizophrenia (Kendler et al., 1993; McGuffin et al., 1995). The overall dose-response pattern is also consistent with the higher fit of a dimensional construct over different levels of categorical definitions.

4.2. Nosological implications

These results suggest that diagnostic conventions for schizophrenia may be arbitrary and not reflective of a natural discontinuity in "schizophrenic" features as presented in a population of psychotic

subjects. In other words, given the continuous distribution of schizophrenia-related variables, it seems rather arbitrary where cutoffs are made between schizophrenic and non-schizophrenic psychoses. Accordingly, schizophrenia may be viewed as the "end-stage" disease or the extreme pole of the psychotic continuum that is characterized by severe and generalized deterioration across a variety of domains (Crow, 1995).

A dimensional schizophrenia construct is consistent with the interpretation that traditional diagnostic systems are the result of both drawing artificial boundaries on a dimensional construct and emphasizing (or de-emphasizing) different phenomenological and clinical aspects of the construct. The dimensional view is also compatible with findings coming from diverse investigative realms. From a statistical perspective, Grove (1991) compared two mathematical strategies (categorical and dimensional) for predicting a criterion variable and showed that over almost all of the parameter space encountered in psychopathology, dimensional prediction of the criterion was superior to taxon-mediated prediction. This finding has been corroborated in psychosis research by a number of recent studies (van Os et al., 1999; Peralta et al., 2002; Rosenman et al., 2003) that have consistently shown the superior validity of dimensional models of schizophrenia over the categorical ones. On the other hand, a body of research (reviewed by van Os et al., 1998) has accumulated suggesting that, within the field of psychotic disorders, a dimensional view of schizophrenia is consistent (or inversely, a categorical view is inconsistent) with findings showing a continuous variation in risk factors, symptoms, outcome and neuroimaging variables. Furthermore, this dimensional view of schizophrenia according to risk factors, phenomenology and pathophysiology may be extended to non-psychotic spectrum disorders such as schizotaxia (Tsuang et al., 2000) and schizotypal personality disorder (Siever and Davis, 2004).

Schizophrenia research and practice would benefit from moving beyond categorical definitions, or at least too narrow ones, of the disorder. They are neither intrinsically reliable (as illustrated by the number and variability of schemes that have been proposed in the last century) nor valid (as demonstrated by the superior validity of dimensional models over categorical ones), and regarding utility, categorical definitions have failed to provide the necessary clarification about differential aetiology, pathophysiology, or treatment. The categorical construct of schizophrenia is so deeply embedded in the history of psychiatric nosology that the several lines of evidence indicating that this conceptualization of the disorder may be problematic have had negligible impact on further developments of this construct. Accordingly, there is an urgent need for a paradigm shift—from a categorical to a dimensional one—in classifying and modeling psychotic disorders. It should be acknowledged, however, that likewise other psychiatric disorders, categorical and dimensional representations of schizophrenia are not antagonistic but complementary, and that the two approaches may have different validity and utility depending on the purpose of the diagnostic procedure (Strauss and Rochester, 1973; Millon, 1991). In this respect, an integrative mixed categorical–dimensional model to assess and classify schizophrenia within psychotic disorders has been recently proposed (Peralta and Cuesta, 2000).

4.3. Strengths and weaknesses of the study

Strengths of the study include the large sample size, the inclusion of patients with different levels of chronicity, and the broad number of diagnosis schemes analyzed covering all the relevant conceptualizations of schizophrenia over the last hundred years. Furthermore, the factor analytical results were validated across different statistical methods and levels of chronicity. Several limitations have to be considered in interpreting our findings. First, the population study was restricted to hospitalized patients, and, therefore, the degree to which the results can be generalized to less severe psychotic patients remains unknown. Second, in interpreting the factor analytical results we relied on the general schizophrenia factor because it explained the largest amount of variance. This factor, however, left unexplained a substantial proportion of the total variance accounted for by the factor analytical solution. The other factors, however, explained little of the variance, and their component items also

loaded on the general schizophrenia factor. And third, the external validity of the dimensional schizophrenia construct based on the general schizophrenia factor cannot be taken for granted given that most of the validating variables were the main defining features of the disorder, which implies a tautological reasoning. Notwithstanding, we also used as validating variables a number of features that have been traditionally linked to schizophrenia and that are not included in any schizophrenia definition, which represents a true external validation procedure, thus providing strong support for the external validity of the dimensional model.

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