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Major psychoses symptomatology: factor analysis of 2241 psychotic subjects

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Abstract Current nosography classifies major psychoses as separate disorders, but their symptomatological presentation during illness episodes largely overlaps and diagnoses may change during a lifetime. Few analyses of major psychoses symptomatology have been performed so far because of the large number of subjects needed to obtain stable factors. The purpose of this study was, therefore, to identify the symptomatologic structure common to major psychoses based on lifetime symptoms. Two thousand and forty-one inpatients affected by schizophrenic (n=1008), bipolar (n=563), major depressive (n=352), delusional (n=108) and psychotic not otherwise specified disorder (n=210) were rated for lifetime symptoms using the Operational Criteria Checklist for Psychotic Illness (OPCRIT) and included in a factorial analysis. Four factors were obtained, the first consisted of excitement symptoms, the second comprised psychotic features (delusions and hallucinations), the third comprised depression and the fourth disorganization. When scored by the OPCRIT checklist, major psychoses symptomatology is composed of excitement, depressive, delusion and disorganization symptoms.

Key words Mood disorder · Depression · Factor analysis · Bipolar disorder · Schizophrenia · Paranoid disorder

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Introduction

Major psychiatric disorders are clearly separate on the basis of clinical, biological, familial and treatment criteria (Kaplan and Sadock, 1995), but during illness episodes a number of symptoms are similar across diagnoses (e. g., delusional symptoms). Those clusters of symptoms are receiving increasing interest as they evidenced a moderate but significant heritability (Burke et al., 1996; Cardno et al., 1997; Cardno et al., 1998; Kendler et al., 1997; Loftus et al., 1998; Van Os et al., 1996; Van Os et al., 1997), are stable over time (Malla et al., 1993 a; Maziade et al., 1996; Rey et al., 1994) and they are correlated with regional anatomical abnormalities (Chua et al., 1997; Schroder et al., 1995). Most important, genetic liabilities have been recently reported for symptom clusters or behavioral traits independently from psychiatric diagnosis (Benjamin et al., 1996; Cloninger, 1994; Cloninger et al., 1996; Ebstein and Belmaker, 1997; Ebstein et al., 1996; Ginsburg et al., 1996; Serretti et al., 2000; Serretti et al., 1999 b). It is therefore important to identify with a reasonable degree of certainty the symptomatologic structures common to major psychoses. Unfortunately most studies have focused on diagnostic homogeneous samples, although it is well known that most psychiatric diagnoses are subject to revision during a lifetime (Chen et al., 1996; Rabinowitz et al., 1994; Rice et al., 1992).

For schizophrenia a number of reports proposed and tested models of one to five underlying latent roots. The one factor model binds all schizophrenia symptoms into one factor with positive and negative symptoms at the extremes (Andreasen and Grove, 1982). The classification of schizophrenia into type I and type II is an example of the two factor model (Crow, 1980), which was also confirmed by a factor analytic study (Mortimer et al., 1990), where 'positive' and 'negative' factors included all symptoms. A three factor model composed of 'negative' (blunted affect, alogia, avolition, anhedonia), 'positive' (hallucinations, delusions), and 'disorganized' (positive

and negative thought disorders, bizarre behavior, inappropriate affect) symptoms was proposed by the majority of researchers, and appeared to be quite stable among different samples (Andreasen et al., 1995; Bilder et al., 1985; Brekke et al., 1994; Cardno et al., 1996; Cuesta and Peralta, 1995; Liddle, 1987; Liddle and Barnes, 1990; Malla et al., 1993 b; Maziade et al., 1995; Palacios-Araus et al., 1995; Peralta et al., 1992; Schroder et al., 1995; Thompson and Meltzer, 1993) though with small differences on factor composition (Bassett et al., 1994). Four factor models present a certain degree of heterogeneity. One study proposed a fourth 'relational' factor (intimacy and closeness, relationships) that was highly correlated with the 'negative' pattern (Peralta et al., 1994), while a depression factor was independent (Willem Van der Does et al., 1995) and, finally the classification premorbid social adjustment deficits was added to the three classical factors (Lenzenweger and Dworkin, 1996). Five factor models have also been proposed with negative, positive, excitement, cognitive and depression/anxiety as separate factors (Lindenmayer et al., 1994; Lindenmayer et al., 1995 a; Lindenmayer et al., 1995 b). Taken together, these studies suggest that schizophrenia is not a unitary syndrome (Dollfus and Everitt, 1998; Kendler et al., 1998).

For mood disorders, fewer reports have been produced. For bipolar disorder, to our knowledge, only the three factor model was detected, composed by the same 'negative', 'positive' and 'disorganized' factors found in schizophrenia (Maziade et al., 1995), while manic states resulted composed by dysphoria, psychomotor acceleration, psychosis, increased hedonic function and irritable aggression (Cassidy et al., 1998; Serretti et al., 1999 c). For major depression, models composed of three distinct factors have also been proposed. Those mainly subdivided depressive and anxiety symptomatology, with a third minor factor regarding behavior (Kendler et al., 1987). We previously identified the delusional and atypical factors as separate from the general depressive factor (Serretti et al., 1998). Further subitem analyses yielded cognitive-vegetative, endogenous-neurotic and retardation-agitation as separate factors (Bech et al., 1993; Carney et al., 1965; Clark et al., 1994; Craighead and Evans, 1996; Galinowski and Lehert, 1995; Maes et al., 1994; Parker et al., 1993; Rassaby and Paykel, 1979).

Heterogeneous psychotic populations have been scarcely studied. The same three factors detected in schizophrenic and bipolar samples were proposed (Klimidis et al., 1993; Maziade et al., 1995; Minas et al., 1994; Minas et al., 1992), but also the five factors composed of manic symptoms, depressive symptoms, negative (defect) symptoms and formal thought disorders, positive (psychotic) symptoms, and catatonic symptoms have been identified (Kitamura et al., 1995). Finally, the largest study performed on 630 subjects identified the three classical factors (Toomey et al., 1997).

Previously, we analyzed a mixed sample composed of 1004 subjects affected by mood and schizophrenic spectrum disorders and we identified the four factors 'Excitement', 'Depression', 'Disorganization' and 'Delusion' (Serretti et al., 1996). We have now expanded that sample, adding a large sample of German psychotic subjects.

The purpose of the present paper was to analyze the symptomatologic structure of major psychoses in the largest sample published so far, to test the stability of our previous finding and to investigate possible differences between the Italian and German populations.

Method

Sample

We collected 2241 subjects (see Table 1 for description of the sample) of Caucasian origin consecutively admitted to the Department of Neuropsychic Sciences of S. Raffaele Hospital in Milan, Italy (DSNP-HSR) and Department of Psychiatry, University of Bonn, Germany. Informed consent to participate was obtained after the procedure had been fully explained. There is a partial overlap of subjects with the previous cohort of 1004 subjects (Serretti et al., 1996) that has been expanded to 1555. All the patients were evaluated using the OPCRIT checklist (McGuffin et al., 1991) and, as suggested by those authors, we applied a lifetime perspective for scoring symptoms (Farmer et al., 1994). OPCRIT comprises a 90-item checklist of signs and symptoms that cover major psychoses symptomatology and a suite of computer programs, which together generate diagnoses according to the operational criteria of 12 major classificatory systems (e. g., DSM-III, DSM-III-R, RDC, ICD-10). The OPCRIT checklist was rated by an experienced psychiatrist on the basis of direct interviews and, when possible, with the aid of previous charts and family informants. OPCRIT is used in a wide range of psychiatric research including both the European Science Foundation and NIMH research initiatives in the molecular genetics of mental disorders. It has been validated on a sample of 100 subjects affected by mood disorders and schizophrenia and good to excellent agreement was achieved between OPCRIT diagnoses and those made by consensus best-estimate procedures (Craddock et al., 1996; Williams et al., 1996). Inter-rater reliability has been evaluated in research centers across Europe and the USA including ours. Each rating was then compared to a standard rating using a kappa statistic. Good levels of reliability were observed within all classifications (e. g., DSM-III-R, kappa = 0.73) and a similar pattern of rating was found in both the European and USA samples (Craddock et al., 1996; Williams et al., 1996).

Subjects lifetime diagnoses were assigned by two independent psychiatrists on the basis of clinical interviews, medical records and complemented with the OPCRIT system according to DSMIV criteria (American Psychiatric Association, 1994). We included all subjects affected by major psychoses, whereas the presence of concomitant diagnoses of mental retardation or drug dependence, together with somatic or neurological illnesses that impaired psychiatric evaluation (e. g., hypothyroidism mimicking a depressive state) represented exclusion criteria. The DSNP-HSR is a specialized institution for the

Table 1 Description of the sample

	ITA	DEU	ALL
Sex M/F	682/873	335/351	1017/1224
Age	42.21±13.96	41.22±12.75	41.72±13.38
Onset	29.78±12.33	25.42±10.42	28.52±11.97
Bipolar	477(30.68 %)	86(12.54 %)	563(25.12 %)
Schizoph.	446(28.68 %)	562(81.92 %)	1008(44.98 %)
Major Depressive	335(21.54 %)	17(2.48 %)	352(15.71 %)
Psyc. NOS	191(12.28 %)	19(2.77 %)	210(9.37 %)
Delusional	106(6.82 %)	2(0.29 %)	108(4.82 %)
All patients	1555	686	2241

treatment of mood disorders and schizophrenia, with 152 acute inpatients and about 10 000 outpatients, and is probably the largest center for psychotic disorders in Europe. Patients gain access from all over Italy by their own volition or following the advice of a general practitioner, but our center is a tertiary structure and therefore we cannot exclude a potential bias associated with severity of illness. Over 10,000 new cases came to our center during the study period, which extended from 1991 to 1998. Of these, 1555 patients satisfied inclusion criteria.

Statistical analysis

The 90 opcrit variables were reduced to 46 for the input of the factoring process. This reduction was conducted following the criteria of:

a) Exclusion of variables not directly related to phenomenology (Source of rating, Time frame, Sex code, Age of onset, Mode of onset, Married, Unemployed, Duration of illness, Poor premorbid work adjustment, Poor premorbid social adjustment, Premorbid personality disorder, Alcohol/drug abuse within one year of onset, Family history of schizophrenia, Family history of other psychiatric disorder, Coarse brain disease prior to onset, Definite psychosocial stressor prior to onset, Relationship psychotic / affective symptoms, Non-affective hallucination in any modality, Information not credible, Lack of insight, Rapport difficult, Impairment/incapacity during disorder, Psychotic symptoms respond to neuroleptics, Course of disorder). b) Exclusion of variables with variance near 0, i. e., scoring 0 for almost all subjects (e. g., Catatonia, Delusions of passivity, Other primary delusions, Delusions of poverty, Nihilistic delusions, Thought echo, Running commentary voices, Other (non-affective) auditory hallucinations, Life time diagnosis of alcohol abuse/dependence, Life time diagnosis of cannabis abuse/dependence, Life time diagnosis of other abuse/dependence, Alcohol abuse/dependence with psychopathology, Cannabis abuse/dependence with psychopathology, Other abuse/dependence psychopathology). c) Exclusion of variables showing high colinearity with other variables, i. e., variables that slightly differ from others (e. g., Restricted affect versus Blunted affect). d) Exclusion of variables highly dependent from drug treatment (Initial insomnia, Middle insomnia (broken sleep), Excessive sleep, Increased appetite, Weight gain).

The factor analysis is explained in detail elsewhere (Serretti et al., 1996). Briefly, an Exploratory Factor Analysis was performed using the Principal Component Analysis method. Because of the ordinal or dichotomous nature of our data, we used a polychoric correlation matrix, since it has been demonstrated that this particular matrix gives more stable parameter estimates when using ordinal or dichotomous variables (Joreskog and Sorbom, 1989). Pairwise exclusion of missing data was applied. The number of factors to be included was defined following the criteria of i) eigenvalues greater than the average, in our case for a polychoric matrix the eigenvalue average is 1; ii) evaluation of the shape of the eigenvalue function, where a strong change on the slope of this function may indicate that any other factor following the abrupt slope variation should be disregarded (all the other factors may represent only distortion of the overall pattern, being mostly only "error factors"). We used both methods because there is not a standard and each one has limitations; in fact the method we used has been criticized by some (Velicer and Fava, 1998; Zwick and Velicer, 1984). Varimax rotation followed.

Results

A description of the sample is reported in Table 1. The eigenvalue distribution is displayed in Fig. 1. A four factor structure gave the best fit and explained 47.1 % of the total variance (Table 2). The first factor, labeled 'excitement' symptoms, explained 20.8 % of the total variance and was a factor in which classical excitement symptoms clustered. The second factor was composed of items describing 'psychotic' symptoms (delusions and hallucinations). The third factor was only composed of 'depression' symptoms and the fourth included mainly 'disorganization' features.

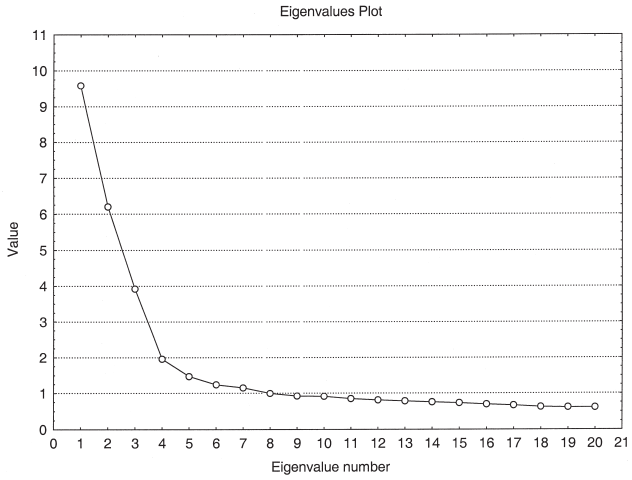

Fig. 1 Eigenvalue distribution.

In order to investigate the hypothesis of a different symptomatology structure between Italian and German subjects, we analyzed the two samples of subjects separately. The factor structure of the two subgroups was, however, similar. In both groups items loaded onto the same factors, with the only difference that in the German sample the symptom 'Dysphoria' loaded mainly on the 'depression' factor compared to a main load on the 'excitement' one in the Italian sample. The eigenvalues in the Italian and German sample, respectively, were 11.55, 6.18, 3.9, 2.0 and 7.03, 5.71, 3.15, 1.99.

Discussion

The present analysis of major psychoses symptomatology yielded four strong factors. The first factor, labeled 'excitement', was composed of the essential features of manic states. The second factor was homogeneously composed of delusion and hallucination items. The third factor comprised depressive symptoms and the fourth disorganization.

To the best of our knowledge this is the largest sample ever analyzed. The main finding is that the enlargement of our previous sample (Serretti et al., 1996) confirmed the factor structure; this was also true when we conducted the analysis separately in an independent sample of the German population.

Comparisons with previous factor analytic studies of major psychoses symptomatology suggest that results are similar, except for the addition of the excitement factor (Maziade et al., 1995), or the lack of many minor factors (Kitamura et al., 1995). The first factor includes classical excitement symptoms. This has been seldom reported, probably due to the low rate of bipolar subjects in published samples. The second factor is comparable to the 'positive' factor described in most studies on mixed

Table 2 Factor loadings of the 46 symptoms extracted from the OPCRIT checklist. Loadings greater than 0.4 are printed in bold

Symptoms	Excitement	Delusion	Depression	Disorganization
Excessive activity	**0.87**	–0.17	0.08	–0.05
Elevated mood	**0.85**	–0.16	0.12	–0.08
Reduced need for sleep	**0.84**	–0.17	0.11	–0.07
Pressured speech	**0.84**	–0.15	0.04	–0.05
Thoughts racing	**0.81**	–0.10	0.10	–0.02
Increased sociability	**0.77**	–0.07	0.11	–0.02
Increased self-esteem	**0.74**	0.03	0.05	–0.13
Distractibility	**0.71**	–0.02	0.08	0.19
Irritable mood	**0.67**	0.01	0.09	0.06
Reckless activity	**0.62**	–0.05	0.13	0.06
Agitated activity	**0.58**	0.09	0.09	0.16
Grandiose delusions	**0.52**	0.25	–0.03	–0.06
Dysphoria	**0.50**	–0.02	0.37	0.08
Persecutory/jealous delusions & hallucinatiog	–0.08	**0.70**	–0.15	0.13
Delusions & hallucinations last for one week	–0.01	**0.70**	–0.11	0.16
Delusions of influence	–0.01	**0.68**	–0.07	0.12
Persecutory delusions	0.030	**0.66**	–0.11	0.03
Widespread delusions	–0.03	**0.63**	–0.06	0.01
Abusive/accusatory/ persecutory voices	–0.13	**0.62**	–0.11	0.18
Third person auditory hallucinations	–0.09	**0.61**	–0.10	0.21
Primary delusional perception	–0.00	**0.57**	0.03	0.17
Well-organized delusions	0.06	**0.57**	0.03	–0.19
Thought insertion	–0.06	**0.50**	–0.06	0.16
Bizarre delusions	–0.04	**0.50**	–0.09	0.33
Thought broadcast	–0.02	**0.49**	0.03	0.08
Thought withdrawal	–0.06	**0.44**	–0.02	0.17
Loss of pleasure	0.06	–0.10	**0.81**	0.00
Loss of energy/ tiredness	0.02	–0.07	**0.76**	0.06
Slowed activity	0.11	–0.04	**0.69**	0.09
Excessive self-reproach	0.10	–0.14	**0.68**	–0.24
Diminished libido	0.02	–0.15	**0.68**	–0.08
Poor appetite	0.07	–0.17	**0.67**	–0.15
Diurnal variation (mood worse mornings)	0.21	–0.16	**0.61**	–0.22
Suicidal ideation	0.11	0.08	**0.59**	–0.08
Poor concentration	0.14	0.04	**0.58**	0.19
Weight loss	0.07	–0.14	**0.58**	–0.10
Early morning waking	0.30	–0.21	**0.55**	–0.21
Delusions of guilt	0.01	0.19	**0.36**	–0.14
Incoherent	0.12	0.14	–0.13	**0.66**
Speech difficult to understand	0.08	0.08	0.07	**0.63**
Inappropriate affect	0.03	0.14	–0.16	**0.56**
Positive formal thought disorder	0.20	0.30	–0.10	**0.54**
Bizarre behavior	0.11	0.35	–0.12	**0.53**
Blunted affect	–0.19	0.12	–0.05	**0.49**
Deterioration from premorbid level of functioning	–0.19	0.44	–0.18	**0.49**
Negative formal thought disorder	–0.17	0.38	–0.01	**0.47**
Explained variance	7.35	5.69	5.39	3.24
Proportion of total variance	0.16	0.12	0.12	0.07
Eigenvalue	9.58	6.20	3.92	1.96

psychotic patients (Kitamura et al., 1995; Maziade et al., 1995; Serretti et al., 1996). The third factor is a 'clean' factor where most depressive items loaded. Our depression factor has some overlap with the negative factor of the literature. However, depressive symptoms are somewhat different from negative symptoms (Brekke et al., 1994; Malla, 1995). In our sample some negative symptoms have been included into the disorganization factor. This finding is in accordance with a reported partial overlap between them (Sax et al., 1996). The last 'disorganization' factor is comparable to previous studies. However, both positive and negative thought disorders loaded on this factor because they were mildly correlated (0.24); this correlation could be due to their very low rate in the affective subjects (30 and 5 % respectively) compared to schizophrenia (67 and 62 %). In fact the correlation between positive and negative thought disorders in schizophrenics is not significant.

The variance explained by the factors was less than 50 %, which indicates that there is substantial heterogeneity among subjects. The low factor/item ratio should, however, be kept in mind, where 46 items were represented by only 4 factors.

Our results are of importance both for the clinician and the researcher. In clinical terms we demonstrated how the same symptomatology may be present in different diagnoses, which is of importance for targeted therapies. The identification of subpopulations of subjects defined by homogeneous symptomatology may be also of particular importance in genetic research or pharmacological studies where homogeneity is crucial. The usefulness of such procedures has already been well established: we were able to detect associations of the dopamine receptors D4 and D2 with a subsample of psychotic subjects that presented psychotic features, while the analysis of the whole sample only yielded negative results (Serretti et al., 2000, 1999 a, 1999 b).

A limitation of the current analysis is that not every psychopathologic symptom has been included and therefore symptom factors reflect the composition of the checklist. In particular, a number of items relating to anxiety symptoms and some negative symptoms were not included. Moreover, as already pointed out in several previous reports, the use of drugs could bias our ability to detect naive symptomatology, but it has been shown that this should not constitute a major obstacle in detecting valid latent structures (Lindenmayer et al., 1995 b; Peralta et al., 1994; Serretti et al., 1996). In particular, studies investigating symptom structures before and after treatment demonstrated that there were no differences in symptom structure across medication status (Harvey et al., 1996). Thus, while most subjects were admitted assuming neuroleptic, lithium, antidepressant or benzodiazepine treatments, we applied a lifetime perspective to rate the OPCRIT checklist, also using complementary sources of information like previous records and family informants. This strategy allowed us to describe early drug-free illness phases, when needed. Indeed factors have been described as quite stable over

time (Addington and Addington, 1991; Eaton et al., 1995; Malla et al., 1993 a; Rey et al., 1994), even if mild changes during the illness have also been described (Arndt et al., 1995; Eaton et al., 1995; Salokangas, 1997). In particular the two dimensions of positive symptoms, psychoticism and disorganization tend to be less stable when compared to negative symptoms (Arndt et al., 1995). We have used the OPCRIT checklist while most studies used different instruments; this was necessary to cover a wide psychopathology area. Thus, although the symptom structures has been described as dependent from the instrument used (Silver et al., 1993), most items are the same across instruments and the only other study using the OPCRIT checklist on schizophrenia identified the three classical factors (Cardno et al., 1996).

In conclusion, major psychoses symptomatology proved to be composed of four factors, namely excitement, depressive, delusion and disorganization symptoms. These factors allow the identification of homogeneous subpopulations of subjects.

References

Addington J, Addington D (1991) Positive and negative symptoms of schizophrenia. Their course and relationship over time. Schizophr Res 5:51–59

American Psychiatric Association (1994) Diagnostic and Statistical Manual of Mental Disorders, 4th Edition. American Psychiatric Association, Washington DC

Andreasen NC, Arndt S, Alliger R, Miller D, Flaum M (1995) Symptoms of schizophrenia. Methods, meanings, and mechanisms. Arch Gen Psychiatry 52:341–351

Andreasen NC, Grove WM (1982) The classification of depression: traditional versus mathematical approaches. Am J Psychiatry 139:45–52

Arndt S, Andreasen NC, Flaum M, Miller D, Nopoulos P (1995) A longitudinal study of symptom dimensions in schizophrenia. Prediction and patterns of change. Arch Gen Psychiatry 52:352–360

Bassett AS, Bury A, Honer WG (1994) Testing Liddle's three-syndrome model in families with schizophrenia. Schizophr Res 12:213–221

Bech P, Malt U, Dencker S, Ahlfors U, Elgen K, Lewander T, Lundell A, Simpson G, Lingjaerde O (1993) Scales for assessment of diagnosis and severity of mental disorders. Acta Psychiatr Scand 87 (Suppl 372):37–40

Benjamin J, Li L, Patterson C, Greenberg B, Murphy D, Hamer D (1996) Population and familial association between the D4 dopamine receptor and measures of Novelty Seeking. Nat Genet 12:81–84

Bilder RM, Mukergee S, Rieder RO, Pandurangi AK (1985) Symptomatic and neuropsychological components of defect state. Schizophrenia Bullettin 11:409–419

Brekke JS, DeBonis JA, Graham JW (1994) A latent structure analysis of the positive and negative symptoms in schizophrenia. Compr Psychiatry 35:252–259

Burke JG, Murphy BM, Bray JC, Walsh D, Kendler KS (1996) Clinical similarities in siblings with schizophrenia. Am J Med Gen 67:239–243

Cardno AG, Holmans PA, Harvey I, Williams MB, Owen MJ, McGuffin P (1997) Factor-derived subsyndromes of schizophrenia and familial morbid risks. Schizophr Res 23:231–238

Cardno AG, Jones LA, Murphy KC, Asherson P, Scott LC, Williams J, Owen MJ, McGuffin P (1996) Factor analysis of schizophrenic symptoms using the OPCRIT checklist. Schizophr Res 22:233–239

Cardno AG, Jones LA, Murphy KC, Sanders RD, Asherson P, Owen MJ, McGuffin P (1998) Sibling pairs with schizophrenia or schizoaffective disorder – associations of subtypes, symptoms and demographic variables. Psychol Med 28:815–823

Carney M, Roth M, Garside R (1965) The diagnosis of depressive syndromes and the prediction of ECT response. Br J Psychiatry 111:659–674

Cassidy F, Forest K, Murry E, Carroll B (1998) A factor analysis of the signs and symptoms of mania. Arch Gen Psychiatry 55:27–32

Chen YR, Swann AC, Burt DB (1996) Stability of diagnosis in schizophrenia. Am J Psychiatry 153:682–686

Chua SE, Wright IC, Poline JB, Liddle PF, Murray RM, Frackowiak RS, Friston KJ, McGuire PK (1997) Grey matter correlates of syndromes in schizophrenia. A semi-automated analysis of structural magnetic resonance images. Br J Psychiatry 170:406–410

Clark D, Steer R, Beck A (1994) Common and specific dimensions of self-reported anxiety and depression: implications for the cognitive and tripartite models. J Abnorm Psychol 103:645–654

Cloninger C (1994) Turning point in the design of linkage studies of schizophrenia. Am J Med Gen 54:83–92

Cloninger C, Adolfsson R, Svrakic N (1996) Mapping genes for human personality. Nat Genet 12:3–4

Craddock M, Asherson P, Owen MJ, Williams J, McGuffin P, Farmer AE (1996) Concurrent validity of the OPCRIT diagnostic system. Comparison of OPCRIT diagnoses with consensus best-estimate lifetime diagnoses. Br J Psychiatry 169:58–63

Craighead W, Evans D (1996) Factor analysis of the Montgomery-Asberg Depression Rating Scale. Depression 4:31–33

Crow TJ (1980) Molecular pathology of schizophrenia: more than one disease process? Br Med J 280:66–68

Cuesta MJ, Peralta V (1995) Psychopathological dimensions in schizophrenia. Schizophr Bull 21:473–482

Dollfus S, Everitt B (1998) Symptom structure in schizophrenia – two-, three- or four-factor models. Psychopathology 31:120–130

Eaton WW, Thara R, Federman B, Melton B, Liang KY (1995) Structure and course of positive and negative symptoms in schizophrenia. Arch Gen Psychiatry 52:127–134

Ebstein RP, Belmaker RH (1997) Saga of an adventure gene: novelty seeking, substance abuse and the dopamine D4 receptor (D4DR) exon III repeat polymorphism. Mol Psychiatry 2:381–384

Ebstein RP, Novick O, Umansky R, Priel B, Osher Y, Blaine D, Bennett ER, Nemanov L, Kats M, Belmaker RH (1996) Dopamine D4 receptor (D4DR) exon III polymorphism associated with the human personality trait of Novelty Seeking. Nat Genet 12:78–80

Farmer AE, Williams J, Jones I (1994) Phenotypic definitions of psychotic illness for molecular genetic research. Am J Med Gen 54:365–371

Galinowski A, Lehert P (1995) Structural validity of MADRS during antidepressant treatment. Int Clin Psychopharmacol 10:157–161

Ginsburg B, Werick T, Escobar J, Kugelmass S (1996) Molecular genetics of psychopathologies: a search for simple answers to complex problems. Behav Genet 26:325–333

Harvey PD, Davidson M, White L, Keefe RS, Hirschowitz J, Mohs RC, Davis KL (1996) Empirical evaluation of the factorial structure of clinical symptoms in schizophrenia: effects of typical neuroleptics on the brief psychiatric rating scale. Biol Psychiatry 40:755–760

Joreskog KG, Sorbom D (1989) LISREL 7 – A Guide to the Program and Applications. SPSS, Chicago

Kaplan HI, Sadock BJ (1995) Comprehensive Textbook of Psychiatry VI. The Williams and Wilkins Company, Baltimore, Maryland

Kendler K, Heat A, Martin N, Eaves L (1987) Symptoms of anxiety and symptoms of depression. Arch Gen Psychiatry 44:451–457

Kendler KS, Karkowski LM, Walsh D (1998) The structure of psychosis – latent class analysis of probands from the Roscommon family study. Arch Gen Psychiatry 55:492–499

Kendler KS, Karkowski-Shuman L, O'Neill FA, Straub RE, MacLean CJ, Walsh D (1997) Resemblance of psychotic symptoms and syndromes in affected sibling pairs from the Irish Study of High-Density Schizophrenia Families: evidence for possible etiologic heterogeneity. Am J Psychiatry 154:191–198

Kitamura T, Okazaki Y, Fujinawa A, Yoshino M, Kasahara Y (1995) Symptoms of psychoses. A factor-analytic study. Br J Psychiatry 166:236–240

Klimidis S, Stuart GW, Minas IH, Copolov DL, Singh BS (1993) Positive and negative symptoms in the psychoses. Re-analysis of published SAPS and SANS global ratings. Schizophr Res 9:11–18

Lenzenweger MF, Dworkin RH (1996) The dimensions of schizophrenia phenomenology. Not one or two, at least three, perhaps four. Br J Psychiatry 168:432–440
Liddle PF (1987) The symptoms of chronic schizophrenia. A re-examination of the positive-negative dichotomy. Br J Psychiatry 151:145–151
Liddle PF, Barnes TRE (1990) Syndromes of chronic schizophrenia. Br J Psychiatry 157:558–561
Lindenmayer JP, Bernstein-Hyman R, Grochowski S (1994) A new five factor model of schizophrenia. Psychiatric Quarterly 65:299–322
Lindenmayer JP, Bernstein-Hyman R, Grochowski S, Bark N (1995 a) Psychopathology of schizophrenia: initial validation of a 5-factor model. Psychopathology 28:22–31
Lindenmayer JP, Grochowski S, Hyman RB (1995 b) Five factor model of schizophrenia: replication across samples. Schizophr Res 14:229–234
Loftus J, DeLisi LE, Crow TJ (1998) Familial associations of subsyndromes of psychosis in affected sibling pairs with schizophrenia and schizoaffective disorder. Psychiatry Res 80:101–111
Maes M, Meltzer H, Cosyns P, Schotte C (1994) Evidence for the existence of major depression with and without anxiety features. Psychopathology 27:1–13
Malla AK (1995) Negative symptoms and affective disturbance in schizophrenia and related disorders. Canadian Journal of Psychiatry – Revue Canadienne de Psychiatrie 40:S55–59
Malla AK, Norman RM, Williamson P (1993 a) Stability of positive and negative symptoms in schizophrenia. Canadian Journal of Psychiatry – Revue Canadienne de Psychiatrie 38:617–621
Malla AK, Norman RM, Williamson P, Cortese L, Diaz F (1993 b) Three syndrome concept of schizophrenia. A factor analytic study. Schizophr Res 10:143–150
Maziade M, Bouchard S, Gingras N, Charron L, Cardinal A, Roy MA, Gauthier B, Tremblay G, Cote S, Fournier C, Boutin P, Hamel M, Merette C, Martinez M (1996) Long-term stability of diagnosis and symptom dimensions in a systemmatic sample of patients with onset of schizophrenia in childhood and early adolescence. II: Postnegative distinction and childhood predictors of adult outcome. Br J Psychiatry 169:371–378
Maziade M, Roy MA, Martinez M, Cliche D, Fournier JP, Garneau Y, Nicole L, Montgrain N, Dion C, Ponton AM (1995) Negative, psychoticism, and disorganized dimensions in patients with familial schizophrenia or bipolar disorder: continuity and discontinuity between the major psychoses. Am J Psychiatry 152:1458–1463
McGuffin P, Farmer A, Harvey I (1991) A polydiagnostic application of operational criteria in studies of psychotic illness. Development and reliability of the OPCRIT system. Arch Gen Psychiatry 48:764–770
Minas IH, Klimidis S, Stuart GW, Copolov DL, Singh BS (1994) Positive and negative symptoms in the psychoses: principal components analysis of items from the Scale for the Assessment of Positive Symptoms and the Scale for the Assessment of Negative Symptoms. Compr Psychiatry 35:135–144
Minas IH, Stuart GW, Klimidis S, Jackson HJ, Singh BS, Copolov DL (1992) Positive and negative symptoms in the psychoses: multidimensional scaling of SAPS and SANS items. Schizophr Res 8:143–156
Mortimer AM, Lund CE, Mc Kenna PJ (1990) The positive-negative dichotomy in schizophrenia. Br J Psychiatry 157:41–49
Palacios-Araus L, Herran A, Sandoya M, Gonzalez de la Huebra E, Vazquez-Barquero JL, Diez-Manrique JF (1995) Analysis of positive and negative symptoms in schizophrenia. A study from a population of long-term outpatients. Acta Psychiatr Scand 92:178–182
Parker G, Hadzi Pavlovic D, Brodaty H, Boyce P, Mitchell P, Wilhelm K, Hickie I, Eyers K (1993) Psychomotor disturbance in depression: defining the constructs. J Affect Disord 27:255–265
Peralta V, Cuesta M, De Leon J (1994) An empirical analysis of latent structures underlying schizophrenic symptoms: a four-syndrome model. Biol Psychiatry 36:726–736
Peralta V, de Leon J, Cuesta MJ (1992) Are there more than two syndromes in schizophrenia? A critique of the positive-negative dichotomy. Br J Psychiatry 161:335–343
Rabinowitz J, Slyuzberg M, Ritsner M, Mark M, Popper M, Ginath Y (1994) Changes in diagnosis in a 9-year national longitudinal sample. Compr Psychiatry 35:361–365
Rassaby E, Paykel E (1979) Factor patterns in depression. A replication study. J Affect Disord 1:187–194
Rey ER, Bailer J, Brauer W, Handel M, Laubenstein D, Stein A (1994) Stability trends and longitudinal correlations of negative and positive syndromes within a three-year follow-up of initially hospitalized schizophrenics. Acta Psychiatr Scand 90:405–412
Rice JP, Rochberg N, Endicott J, Lavori PW, Miller C (1992) Stability of psychiatric diagnoses. An application to the affective disorders. Arch Gen Psychiatry 49:824–830
Salokangas RK (1997) Structure of schizophrenic symptomatology and its changes over time: prospective factor-analytical study. Acta Psychiatr Scand 95:32–39
Sax KW, Strakowski SM, Keck PE, Jr., Upadhyaya VH, West SA, McElroy SL (1996) Relationships among negative, positive, and depressive symptoms in schizophrenia and psychotic depression. Br J Psychiatry 168:68–71
Schroder J, Buchsbaum MS, Siegel BV, Geider FJ, Niethammer R (1995) Structural and functional correlates of subsyndromes in chronic schizophrenia. Psychopathology 28:38–45
Serretti A, Lattuada E, Cusin C, Macciardi F, Smeraldi E (1998) Analysis of depressive symptomatology in mood disorders. Depress Anxiety 8:80–85
Serretti A, Lattuada E, Lorenzi C, Lilli R, Smeraldi E (2000) Dopamine receptor D2 ser/cys 311 variant is associated with delusion and disorganization symptomatology in major psychoses. Mol Psychiatry 5:270–274
Serretti A, Lilli R, Di Bella D, Bertelli S, Nobile M, Novelli E, Catalano M, Smeraldi E (1999 a) Dopamine receptor D4 gene is not associated with major psychoses. Am J Med Gen 88:486–491
Serretti A, Macciardi F, Catalano M, Bellodi L, Smeraldi E (1999 b) Genetic variants of dopamine receptor D4 and psychopathology. Schizophr Bull 25:609–618
Serretti A, Macciardi F, Smeraldi E (1996) Identification of symptomatologic patterns common to major psychoses: proposal for a phenotype definition. Am J Med Gen 67:393–400
Serretti A, Rietschel M, Lattuada E, Krauss H, Held T, Nothen M, Smeraldi E (1999 c) Factor analysis of Mania. Arch Gen Psychiatry 56:671–672
Silver H, David D, Kaplan M, Hadjez J, Tubi N, Darnel A, Calev A, Lerer B (1993) Factor analysis of schizophrenic symptoms and comparison of different rating scales. Schizophr Res 10:67–75
Thompson PA, Meltzer HY (1993) Positive, negative, and disorganisation factors from the Schedule for Affective Disorders and Schizophrenia and the Present State Examination. A three-factor solution. Br J Psychiatry 163:344–351
Toomey R, Kremen WS, Simpson JC, Samson JA, Seidman LJ, Lyons MJ, Faraone SV, Tsuang MT (1997) Revisiting the factor structure for positive and negative symptoms: evidence from a large heterogeneous group of psychiatric patients. Am J Psychiatry 154:371–377
Van Os J, Fahy TA, Jones P, Harvey I, Sham P, Lewis S, Bebbington P, Toone B, Williams M, Murray R (1996) Psychopathological syndromes in the functional psychoses: associations with course and outcome. Psychol Med 26:161–176
Van Os J, Marcelis M, Sham P, Jones P, Gilvarry K, Murray R (1997) Psychopathological syndromes and familial morbid risk of psychosis. Br J Psychiatry 170:241–246
Velicer WF, Fava JL (1998) Effects of variable and subjects sampling on factor pattern recovery. Psychol Methods 3:231–251
Willem Van der Does AJ, Dingemans PM, Linszen DH, Nugter MA, Scholte WF (1995) Dimensions and subtypes of recent-onset schizophrenia. A longitudinal analysis. J Nerv Ment Dis 183:681–687
Williams J, Farmer AE, Ackenheil M, Kaufmann CA, McGuffin P (1996) A multicentre inter-rater reliability study using the OPCRIT computerized diagnostic system. Psychol Med 26:775–783
Zwick WR, Velicer WF (1984) A comparison of five rules for determining the number of components in data sets. Psychol Bull 99:432–442