Probing the boundaries of the Kraepelinian dichotomy: Evidence for a transdiagnostic psychosis spectrum encompassing schizophrenia and bipolar disorder

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Abstract

Background: In recent years, the Kraepelinian dichotomy has been challenged in light of evidence on shared genetic and environmental factors for schizophrenia and bipolar disorder, but empirical efforts to identify a transdiagnostic phenotype of psychosis remain remarkably limited.

Aims: To investigate whether schizophrenia spectrum and bipolar disorder lie on a transdiagnostic spectrum with overlapping non-affective and affective psychotic symptoms.

Methods: Multidimensional item response modelling was conducted on symptom ratings of the OPCRIT system in 1168 patients with schizophrenia spectrum and bipolar disorder.

Results: A bifactor model with one general, transdiagnostic psychosis dimension underlying affective and non-affective psychotic symptoms and five specific dimensions of positive, negative, disorganized, manic, and depressive symptoms provided the best model fit and diagnostic utility for categorical classification.

Conclusions: Our findings provide support for including dimensional approaches into classification systems and a directly measurable clinical phenotype for cross-disorder investigations into shared genetic and environmental factors of psychosis.

Introduction

The dichotomy of dementia praecox/schizophrenia and manic depression has informed diagnostic classification in psychiatry ever since it was first proposed by Emil Kraepelin.[1] While this dichotomy remains in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5.0),[2] the need for a dimensional approach to classification in psychiatry,[3] and inclusion of such an approach in updated versions of DSM-5.0[4] and the impending, *eleventh revision of the International Classification of Diseases* (ICD-11),[5] continues to be debated in view of calls for research that looks across diagnostic categories[3,5] and the persistent challenge of high comorbidity rates.[3-8]

In recent years, the Kraepelinian dichotomy has been challenged in light of evidence on common aetiological factors in schizophrenia and bipolar disorder.[9] Evidence has accumulated that genetic risk is partly shared between schizophrenia and bipolar disorder.[9-12] For instance, molecular genetic studies point to common DNA variants that impact on risk of both disorders.[11] There is also evidence on shared environmental contributions to schizophrenia and bipolar disorder.[12] These include prenatal factors,[13,14] childhood adversity,[15] substance misuse,[16,17] urbanicity,[18,19] and ethnicity.[19] These findings, taken together, challenge Kraepelin's[1] distinction between schizophrenia and bipolar disorder and their classification as separate diagnostic entities. Alternatively, Craddock and Owen[9] have proposed a transdiagnostic, mood-psychosis clinical dimension with three overlapping broad domains of psychopathology, namely schizophrenia, schizoaffective and bipolar disorder.

However, there is also evidence on genetic and environmental risks that are not shared between schizophrenia and bipolar disorder. Family studies have consistently reported unique genetic contributions to schizophrenia and bipolar disorder.[12] Findings further suggest some degree of specificity of environmental exposures.[8,18,19] While, coupled with evidence on differences in course and outcome,[8] these findings support the heterogeneity of psychotic disorders, it remains unclear which general and/or specific domains of the clinical psychosis phenotype will be most useful to

measure and map onto genetic and environmental factors and their underlying biological and psychological mechanisms.[9]

Intriguingly, empirical efforts to identify a more fundamental, transdiagnostic phenotype of psychosis at the clinical symptom level remain remarkably limited. While previous factor-analytic work has largely pointed toward a pentagonal model with five dimensions of positive symptoms, negative symptoms, cognitive disorganization, mania, and depression,[20] we have recently reported evidence for a bifactor model that includes one general psychosis dimension underlying affective and non-affective psychotic symptoms as well as five specific psychosis dimensions of positive symptoms, negative symptoms, disorganization, mania, and depression.[21] However, findings were restricted to samples of schizophrenia spectrum disorder and the clinical symptom measure (i.e., the Positive and Negative Syndrome Scale) not directly linked to existing diagnostic classification systems. Also, in contrast to our recent finding, Russo et al.[22] reported a model with two distinct factors for non-affective and affective psychosis. Empirical evidence on general and/or specific symptom dimensions, and their diagnostic utility, in both schizophrenia spectrum *and* bipolar disorder may help psychiatry move toward diagnostic approaches that better match shared and non-shared genetic and environmental risks, on the basis of which treatment and prognosis can be optimised. In this study, we aimed to investigate whether schizophrenia spectrum and bipolar disorders lie on a transdiagnostic spectrum with overlapping non-affective and affective psychotic symptoms using a symptom measure that can be directly used for making clinical diagnosis, i.e., the OPerational CRITeria (OPCRIT) system.[23] To this end, we sought to examine: a) whether the previously identified general psychosis dimension holds across diagnostic categories of schizophrenia spectrum and bipolar disorders; b) whether formation of specific psychosis dimensions is justified in addition to a general psychosis dimension; c) the diagnostic utility of general and specific psychosis dimensions for classifying patients correctly into categorical diagnoses of psychotic disorders; and d) associations between clinical variables and general and specific psychosis dimensions.

Method

Sample

We analysed a pooled sample obtained from the UK700 study[24] and the Bipolar Association Case-Control Study (BACCS).[25] Patients in the UK700 study were recruited between 1994 and 1996 from four UK inner-city mental health services in London and Manchester using the following inclusion criteria: 1) aged between 18 and 65 years; 2) a psychotic illness for at least 2 years. A total of 708 patients were recruited during the study period. Of these, 691 patients with a diagnosis of schizophrenia (n=345), schizoaffective disorder (n=270), mania/bipolar disorder (n=34), and unspecified functional psychoses (n=42) were included into the current study. Patients with a diagnosis of major depression (n=16) or without diagnosis (n=1) were excluded.

Patients for the BACCS study[25] were recruited between 2004 and 2007 from the greater London area, UK, through out-patient psychiatric clinics, self-help groups, and media advertisements. Inclusion criteria were: 1) aged over 18 years; 2) at least two episodes of illness, at least one of which fulfilled diagnostic criteria for mania/hypomania. During the study period, a total of 512 patients were recruited at the London site. Of these, 477 patients with a current diagnosis of mania/bipolar disorder (n=332), hypomania (n=143), and unspecified functional psychosis (n=2) were included in the current study. Patients with a current diagnosis of major depression (n=2) and current unspecified diagnosis (n=33) were excluded. More detailed information including ethical approval for all relevant aspects of the studies is available in Burns et al.[24] and Cohen-Woods et al.[25]. The two samples were combined in a pooled sample to achieve both sufficient numbers in each diagnostic group and a sufficient prevalence of individual symptoms for item response model analysis to be performed.

Measures

The OPCRIT system was used to assess psychiatric symptoms as described by McGuffin et al.[23] OPCRIT consists of a 90-item checklist that allows for structured examination of basic demographic information, disease course and severity (including age at onset, mode of onset, premorbid adjustment), and psychotic symptoms based on all available sources including case records, clinical and research interviews. It provides definitions for each item and algorithms for objective diagnosis of non-affective and affective psychotic disorders based on a range of diagnostic classification systems. A detailed description of the use of OPCRIT in the BACCS and UK700 study is provided in Appendix DS1 in the online data supplement. For the purposes of this study, psychiatric diagnosis was made based on the Research Diagnostic Criteria (RDC) using the OPCRIT system (26), which has been found to be both feasible and reliable in research settings and recently been redesigned for use in clinical settings (i.e., OPCRIT+).[23,27] We used all OPCRIT items with sufficient prevalence of psychotic symptoms (>10%) in the pooled sample for item response model analysis.

Statistical analysis

Multidimensional item response modeling was conducted using the mirt package of the R environment[28] for model estimation. We assumed data to be missing at random, which allowed for inclusion of the full sample. We examined model fit using the log-likelihood (LL), the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and the Sample-size Adjusted BIC (SABIC).[29] For these fit statistics, lower values than for the comparison model indicate a statistically better model fit. In order to examine whether there is a general psychosis dimension and, in addition, whether there are 5 specific symptom dimensions (positive symptoms, negative symptoms, disorganization, mania, depression), we estimated five alternative item response models (Figure DS1): first, a simple unidimensional model with 1 general factor explaining all OPCRIT symptom ratings (model A; corresponding to a unitary psychosis model); second, a multidimensional model with 5 uncorrelated specific factors for each specific symptom dimension (model B); third, a multidimensional model with 5 correlated specific factors (model C; corresponding, as model B, to

the pentagonal model of psychosis[20]); fourth, a bifactor model with 2 distinct factors for affective and non-affective psychosis and 5 uncorrelated factors for each specific symptom dimension (model D; corresponding to the Russo et al.[22] model) and, fifth, a bifactor model with 1 general factor independent from 5 uncorrelated (orthogonal) specific factors (Model E; corresponding to the bifactor model reported in our earlier study of patients with schizophrenia spectrum disorder[21]). The procedure for fitting these models in the context of psychotic symptom ratings have been described in more detail elsewhere.[21] Importantly, the bifactor model with 1 general and 5 specific factors constrained each OPCRIT item to have a nonzero loading on the general factor (i.e., psychosis) and a nonzero loading on a specific factor (e.g., positive symptoms) to examine whether there is a general dimension underlying symptoms of schizophrenia spectrum and bipolar disorder independent from (i.e., non-redundant with) the previously reported specific symptom dimensions. In order to examine the extent to which factor scores of general and specific psychosis dimensions (as predictor variable) allow for accurate classification of patients into diagnostic categories (as outcome variable), multinomial Receiver Operating Characteristic (ROC) analysis[30] were conducted in Stata version 12.[31] Finally, we used linear regression to investigate associations between clinical variables (including age at onset, mode of onset, premorbid work adjustment, and premorbid social adjustment) and factor scores of general and specific psychosis dimensions.

Results

Basic sample characteristics

Basic sample characteristics of the pooled sample of 1168 patients are summarised in Table DS1 in the online data supplement. The mean age at interview was 42.1 years and approximately half were female (n=608, 52.1%). The mean age at illness onset was 22.2 years. The most common diagnosis was mania/bipolar disorder (31.3%), followed by schizoaffective disorder (29.5%) and schizophrenia (23.1%). As can be seen in Table DS2 in the online data supplement, the prevalence of psychotic

symptoms was sufficient in the pooled sample for item response model analysis. Consistent with inclusion criteria, we observed differences in prevalence of symptoms across studies.

Dimensionality of schizophrenia spectrum and bipolar disorder

Model fit statistics for the five alternative dimensional models of schizophrenia spectrum and bipolar disorder are shown in Table 1. The best model fit was consistently observed across model fit statistics for the bifactor model including 1 general and 5 specific symptom factors as compared with all other models. This indicated that there was a general psychosis dimension that explained associations among all symptoms of schizophrenia spectrum and bipolar disorder as well as that, over and above this general psychosis dimension, the formation of 5 specific psychosis dimensions was justified.

[Insert Table 1 here]

Association of symptom ratings with general and specific psychosis dimensions

Table 2 shows standardized factor loadings for the best-fitting model including one general and five specific psychosis dimensions. Factor loadings on the general psychosis factor were moderate to strong for most OPCRIT symptom ratings. OPCRIT ratings of manic symptoms were inversely related to the underlying general psychosis dimension. By contrast, factor loadings of almost all other ratings were in the positive range. Coupled with findings on model fit statistics reported above, this indicated that there is a general psychosis dimension underlying affective and non-affective psychotic symptoms that holds across schizophrenia spectrum and bipolar disorder. We further found weak to moderate factor loadings of OPCRIT ratings on the specific positive, negative and disorganized symptom factor. OPCRIT ratings of manic and depressive symptoms were moderately to strongly associated with the underlying specific symptom dimensions. These findings were first probed in a sensitivity analysis to examine replicability of findings by a bootstrap procedure (Table DS3 in the online data supplement). For those parameters for which some relevant bias was

detected, absolute values of parameters were estimated to be even larger than the respective point estimate.

[Insert Table 2 here]

Diagnostic utility of general and specific psychosis dimensions

All latent factor scores were strongly and positively associated with weighted OPCRIT sum scores for general and specific psychosis dimensions (Table 3). This indicated that higher weighted sum scores on a particular dimension can be interpreted as representations of higher latent factor scores.

[Insert Table 3 here]

Symptom profiles for, and findings on differences in, general and specific psychosis dimensions by diagnostic categories are shown in Figure 1 and Table 3, respectively. Scores on the general psychosis (R^2=0.81), specific positive (R^2=0.04), negative (R^2=0.02), and disorganized (R^2=0.05) symptom dimensions were higher for categorical diagnoses of schizophrenia and schizoaffective disorder compared with bipolar disorder. On the manic symptom dimension, scores were lower for schizophrenia than for bipolar disorder (R^2=0.20). Compared with bipolar disorder, scores on the depressive symptom dimension were higher for schizoaffective disorder and lower for schizophrenia (R^2=0.18).

[Insert Figure 1 here]

We next examined the utility of general and specific psychosis dimensions for predicting categorical diagnoses using multinomial ROC analysis. Findings on classifying patients into diagnostic categories based on general psychosis dimension compared with classifying patients by chance are shown in

Figure DS2 in the online data supplement. Factor scores of the general psychosis dimension yielded a higher proportion of correctly classified patients than each of the specific symptom dimensions alone (Figure DS2a). However, the proportion of patients correctly classified into diagnostic categories based on factor scores of both general *and* specific psychosis dimensions was markedly higher (95% CI 0.69-0.79) than the proportions based on the general psychosis dimension only (95% CI 0.45-0.63), all specific psychosis dimensions combined (95% CI 0.46-0.57), and what would be expected by chance (95% CI 0.24-0.35) (Figure DS2b). Table DS4 in the online data supplement shows corresponding findings from the multinomial regression model with the highest classification accuracy including both general and specific psychosis dimensions for predicting categorical diagnoses.

General and specific psychosis dimensions by clinical variables

Finally, we examined general and specific psychosis dimensions in relation to clinical variables. Findings on factors scores of general and specific psychosis dimensions by age at onset, mode of onset, premorbid work and social adjustment are shown in Table 3. Scores on the general psychosis dimension were significantly higher for patients with a later age at onset, gradual and insidious (vs. acute) mode of onset, poor premorbid work and social adjustment. Table 3 further shows that, compared with patients with an acute onset, those with an insidious onset had lower scores on the positive symptom dimension and higher scores on the negative and depressive symptom dimension. Higher scores on the positive, negative, and disorganized symptom dimension and lower scores on the manic symptom dimension were found in patients with poor premorbid work adjustment. Patients with poor premorbid social adjustment also scored higher on the negative and disorganized symptom dimension than those with good premorbid social adjustment.

Discussion

Principal findings

This study is the first to provide evidence for a general psychosis dimension underlying affective and non-affective psychotic symptoms that holds across schizophrenia spectrum and bipolar disorder. Further, there was evidence to suggest formation of specific psychosis dimensions of positive symptoms, negative symptoms, disorganization, mania, and depression is justified. Symptom profiles revealed that general and specific psychosis dimensions discriminated well between, and were consistent with the typical clinical picture of, categorical diagnoses of psychotic disorders. We also found strong evidence on the diagnostic utility when using both general and specific psychosis dimensions for predicting categorical diagnoses. Finally, there was evidence that general and specific psychosis dimensions were differentially associated with age at onset, mode of onset, premorbid work and social adjustment.

Methodological considerations

We investigated the dimensionality of psychosis in a pooled sample of patients with schizophrenia, schizoaffective disorder, bipolar disorder, hypomania, and unspecified functional psychosis. While this sample allowed for multidimensional item response modelling of psychotic symptom ratings using a clinical measure directly linked to existing diagnostic classification systems, we were able to include only 3 OPCRIT items with sufficient prevalence (>10%) on negative symptoms, resulting in reduced coverage of this domain, which likely accounted for the limited predictive value of this dimension for categorical diagnoses. Further, given these restrictions on prevalence, the pooled sample size did not provide sufficient power for cross-validation of findings. However, single cross-validations are known to make inefficient use of the data.[32] Therefore, we used a bootstrap procedure,[33] providing good evidence on the replicability of findings (Table DS3). Differences in inclusion criteria, OPCRIT rating procedure (Appendix DS1), and prevalence of symptoms (Table DS2) across the two studies, which we purposefully combined in order to achieve sufficient spread in the distribution of non-affective and affective psychotic symptoms, may have led to an artificial increase in variance of both manifest symptoms and latent variables.[34] Even though difficult to disentangle in

this study, we would argue that, given OPCRIT is a well-validated tool purposefully designed to allow flexibility in its use (Appendix DS1)[23,27,42] as well as the underlying commonalities in phenomenology, aetiology, and severity of schizophrenia and bipolar spectrum disorder, such an increase in variance was unlikely to be artificial and instead allowed us to cover a broad range of psychotic disorders. However, ultimately, further investigations that purposefully sample across diagnoses with the same diagnostic assessment methodology are warranted to more fully elucidate this question.[3] Finally, the current study did not include patients with other relevant non-psychotic disorders, which would have helped to disentangle overlap with, or independence from, other important spectra of mental disorder.[4,9,34] Multidimensional item response modelling allowed us to advance on previous research investigating the dimensionality of psychosis by identifying latent dimensions as determinants of symptoms. This approach is now widely considered preferable (e.g. over principal component analysis), let alone, ignoring the dimensional structure and factorial validity of symptom measures altogether, as common causes and liabilities plausibly lead to symptoms, and not vice versa.[34] It is also noteworthy that the bifactor model with 1 general and 5 specific factors consistently provided a better model fit even when compared with models requiring estimation of the same number of free parameters and, therefore, of identical parsimony.[22]

Comparisons with previous research

Recent years have seen calls for research cutting across boundaries of diagnostic categories, in order to strengthen the evidence base for including dimensional approaches in updated versions of DSM-5.0.[3,4,9] Our finding of a general psychosis dimension provides evidence, at the clinical symptom level, that cuts across boundaries of the Kraepelinian dichotomy and suggests that schizophrenia and bipolar disorder lie on a transdiagnostic psychosis spectrum with overlapping non-affective and affective symptoms. When directly compared with a model with two distinct factors for non-affective and affective psychosis (a model of identical parsimony),[22] a superior fit was evident for the bifactor model including 1 general psychosis factor (and 5 specific symptom factors). This extends our

previous finding of a general psychosis dimension[21] in schizophrenia spectrum disorder to individuals with bipolar disorder. This dimension resembles, to a degree, the thought disorder factor reported by previous studies,[7,35] however, the thought disorder factor also included other disorders such as schizotypal and schizoid personality disorders or obsessive-compulsive disorders.[7,35] Consistent with numerous previous studies,[20,21] there was also evidence that, in addition to this dimension, psychotic symptom ratings are best accounted for by 5 specific dimensions of positive symptoms, negative symptoms, disorganization, mania, and depression.

In recent years, some researchers have proposed combining dimensional and categorical approaches in the classification of mental disorders,[4,20] such as ICD-11[5] and (updated versions of) the DSM-5.0.[2] However, to date, there has only been very limited evidence on the diagnostic utility of dimensional representations of psychosis for classifying patients into categorical diagnoses. Overall, strong diagnostic utility of the general and specific psychosis dimensions for allocating patients to diagnoses was demonstrated with the OPCRIT system, a clinical symptom measure that can be used to implement scoring algorithms in both research and routine care.[23,27] Symptom profiles showed that the general psychosis dimension enabled individuals to be placed on the mania (bipolar disorder/hypomania) versus schizophrenia (schizoaffective disorder/schizophrenia) end of the psychosis spectrum. For the specific psychosis dimensions, symptom profiles were consistent with operational definitions of current classification systems[2,36] and remarkably similar to those hypothesized for typical patients.[20] Based on these findings, specific scoring rules can be defined and implemented that allow more accurate classification of patients into these diagnoses. Our findings on symptom profiles may provide a basis for such an approach (Figure DS3): first, quantitative scores on the general psychosis dimension may be used to determine whether to place patients on the mania or schizophrenia end of the psychosis spectrum; in a second step, based on the profiles for specific symptom dimensions, patients may be classified into specific diagnoses.

Findings on differential associations between clinical variables and general and specific psychosis dimensions echoed previous reports.[7,20,21,37] A later, more insidious mode of onset and a poorer premorbid adjustment were associated with the non-affective end of the psychosis spectrum, whereas an earlier, more acute mode of onset and a better premorbid adjustment related to the affective end of the psychosis spectrum (Figure DS3). A similar pattern was also evident for the relationship between these variables and the specific symptom dimensions. There is growing evidence that genetic variation and environmental exposures are shared across diagnostic categories.[11,12] Using the OPCRIT system to derive RDC diagnosis in a twin study, Cardno et al.[10] found evidence of both common and syndrome-specific genetic contributions to psychosis liability. Given also recent calls for identifying cross-cutting dimensions,[3,4] it is intriguing to speculate whether the general schizophrenia-bipolar disorder psychosis dimension that we have identified here might be strongly linked to shared genetic and environmental risks,[9-19,37-39] whereas the specific psychosis dimensions are associated with non-shared risks. While a few studies have investigated intermediate and clinical phenotypes across several different psychotic disorders,[40] to date, no study that we are aware of has identified and validly measured a transdiagnostic, clinical phenotype of general psychosis underlying affective and non-affective psychotic symptoms in schizophrenia and bipolar disorders. However, ultimately, such a measure, as provided here, is required if we are to move from intermediate to clinical phenotypes and study these in relation to course and outcome of psychosis.

Conclusions

Our findings suggest that schizophrenia spectrum and bipolar disorders lie on a transdiagnostic psychosis spectrum with overlapping affective and non-affective psychotic symptoms. Coupled with strong evidence on diagnostic utility, this finding should inform inclusion of dimensional approaches into (updated versions of) the DSM and may substantially enhance classification accuracy of current diagnostic classification systems. Our findings also provide a directly measurable clinical phenotype for cross-disorder investigations into genetic and environmental factors of psychosis. These are now

required to identify shared genetic and environmental contributions to this phenotype (as well as non-shared factors of specific psychosis dimensions) and to disentangle potential overlap with, or independence from, other important spectra of mental disorder.

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Table 1. Model fit statistics unidimensional, multidimensional, and bifactor models in schizophrenia spectrum and bipolar disorder

	Full information fit statistics†				
	LL	**FP**	**AIC**	**BIC**	**SABIC**
Unidimensional (unitary) model (A)	-24624.19	98	49444.39	49940.57	49629.29
Multidimensional (pentagonal) model with uncorrelated factors (B)	-23585.87	98	47367.74	47863.92	47552.64
Multidimensional (pentagonal) model with correlated factors (C)	-22468.5	108	45153.00	45175.23	45356.76
Bifactor model with 2 factors for affective and non-affective psychosis and 5 specific symptom factors (D)	-22539.24	147	45372.49	46116.75	45415.14
Bifactor model with 1 general psychosis and 5 specific symptom factors (E)	-22058.87	147	44411.75	45156.02	44689.09

Note: LL, Log-Likelihood; FP, Free Parameters; AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; SABIC, Sample size Adjusted Bayesian Information Criterion

† A difference of 10 in AIC, BIC, and SABIC is considered important

‡ The best model fit was still observed for model E as compared with a bifactor model, in which factor loadings of mania items on the general factor were fixed to zero and the specific mania factor correlated with the general and other specific factors (LL=-22104.99, AIC=44491.98, BIC=45205.87, SABIC=44758.01; $r_{general\text{-}mania}$=-0.68, $r_{positive\text{-}mania}$=-0.14; $r_{negative\text{-}mania}$=-0.27; $r_{disorganization\text{-}mania}$=0.21; $r_{mania\text{-}depression}$=0.15)

Table 2. Standardized factor loadings in bifactor model

OPCRIT Items	Item no.	Factor loadings						h^2
		General	Positive symptoms	Negative symptoms	Disorganization	Mania	Depression	
Persecutory delusions	54	0.90	0.21					0.86
Well organised delusions	55	0.93	-0.08					0.88
Delusions of influence	58	0.31	0.44					0.29
Bizarre delusions	59	0.91	-0.05					0.84
Widespread delusions	60	0.97	-0.06					0.94
Delusions of passivity	61	0.78	0.37					0.74
Delusions & hallucinations for 1 week	64	0.91	0.34					0.94
Persecutory delusions & hallucinations	65	0.91	0.30					0.91
Thought insertion	66	0.74	0.55					0.84
Thought withdrawal	67	0.80	0.42					0.82
Thought broadcast	68	0.72	0.49					0.76
Third person auditory hallucinations	73	0.78	0.40					0.77
Running commentary voices	74	0.67	0.45					0.65
Abusive/accusatory/persecutory voices	75	0.83	0.30					0.78
Other auditory hallucinations	76	0.77	0.02					0.59
Non-affective hallucination any modality	77	0.79	0.13					0.64
Negative formal thought disorder	29	0.77		0.35				0.71
Restricted affect	32	0.81		0.42				0.82
Blunted affect	33	0.84		0.42				0.88
Bizarre behaviour	17	0.82			0.28			0.75
Speech difficult to understand	26	0.76			0.57			0.91
Incoherent	27	0.70			0.65			0.91
Positive formal thought disorder	28	0.80			0.48			0.87
Inappropriate affect	34	0.73			0.25			0.59
Excessive activity	19	-0.56				0.66		0.75
Reckless activity	20	-0.31				0.54		0.39
Distractibility	21	-0.34				0.62		0.50
Reduced need for sleep	22	-0.63				0.61		0.76
Pressured speech	30	-0.58				0.68		0.81
Thoughts racing	31	-0.72				0.62		0.89
Elevated mood	35	-0.73				0.61		0.90
Irritable mood	36	-0.01				0.54		0.29
Increased sociability	53	-0.54				0.63		0.68
Increased self esteem	56	-0.51				0.65		0.69
Grandiose delusions	57	-0.09				0.66		0.45
Slowed activity	24	0.54					0.62	0.67
Loss of energy/tiredness	25	0.56					0.70	0.81
Dysphoria	37	0.65					0.61	0.80
Loss of pleasure	39	0.51					0.76	0.84
Altered libido	40	0.49					0.67	0.69
Poor concentration	41	0.47					0.61	0.59
Excessive self reproach	42	0.36					0.80	0.78
Suicidal ideation	43	0.64					0.54	0.70
Initial insomnia	44	0.29					0.58	0.42
Middle insomnia (broken sleep)	45	0.46					0.53	0.50
Early morning waking	46	0.07					0.69	0.48
Poor appetite	48	0.00					0.61	0.37
Weight loss	49	-0.21					0.55	0.34
Increased appetite	50	-0.28					0.05	0.08

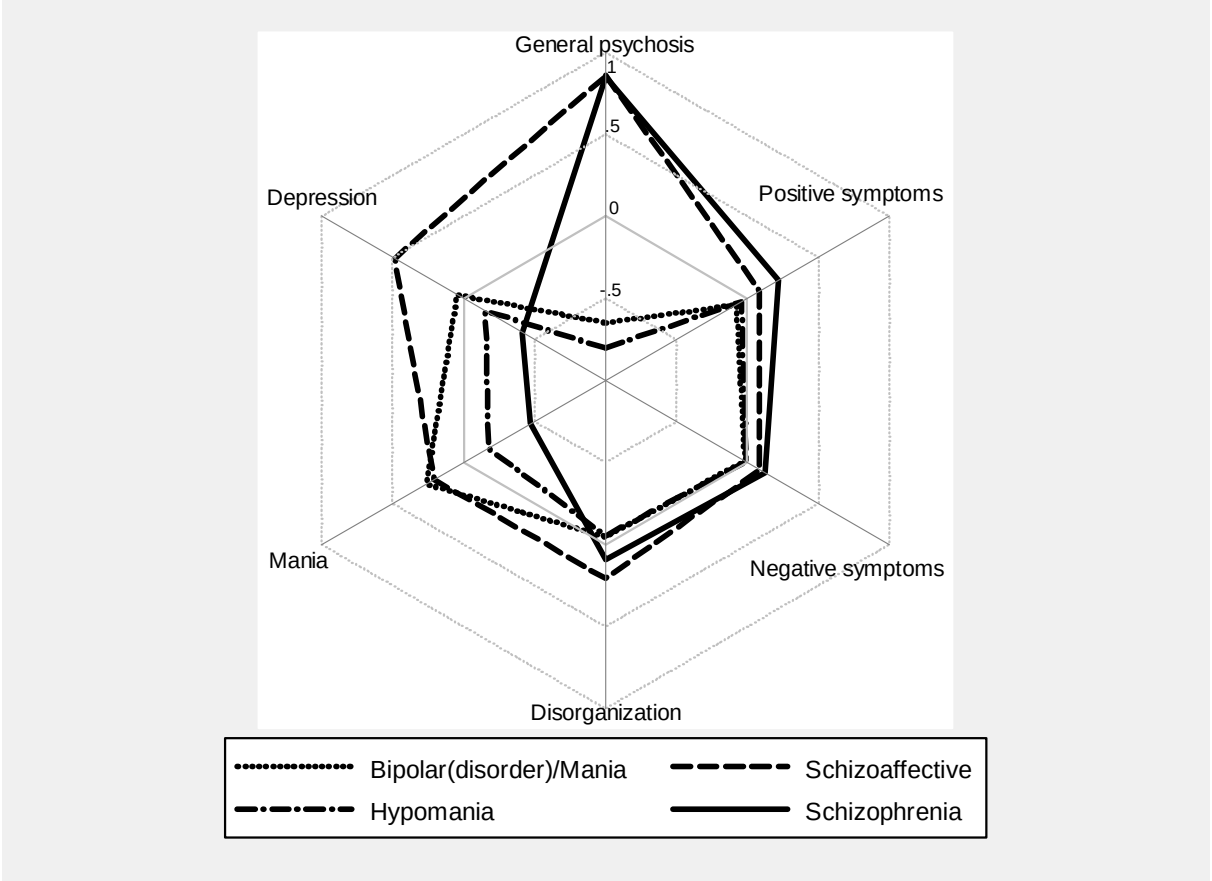
Table 3. Factors scores of general and specific symptom dimensions by clinical variables

	Latent factor scores											
	General		Positive symptoms		Negative symptoms		Disorganisation		Mania		Depression	
	r (95% CI)	p	r (95% CI)	p	r (95% CI)	p	r (95% CI)	p	r (95% CI)	p	r (95% CI)	p
OPCRIT weighted sum scores†												
General	0.93 (0.92-0.94)	<0.001										
Positive symptoms			0.77 (0.74-0.79)	<0.001								
Negative symptoms					0.78 (0.76-0.80)	<0.001						
Disorganization							0.67 (0.64-0.70)	<0.001				
Mania									0.81 (0.79-0.83)	<0.001		
Depression											0.87 (0.86-0.89)	<0.001
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
RDC diagnosis‡												
Hypomania	-0.15 (-0.23 - -0.08)	<0.001	0.04 (-0.08-0.16)	0.551	0.01 (-0.08-0.10)	0.848	-0.01 (-0.11-0.10)	0.907	-0.44 (-0.57 - -0.31)	<0.001	-0.20 (-0.33 - -0.06)	0.005
Schizoaffective disorder	1.50 (1.45-1.56)	<0.001	0.16 (0.07-0.26)	<0.001	0.10 (0.04-0.17)	0.002	0.25 (0.17-0.33)	<0.001	-0.05 (-0.15-0.05)	0.292	0.44 (0.34 - 0.55)	<0.001
Schizophrenia	1.50 (1.44-1.56)	<0.001	0.30 (0.20-0.40)	<0.001	0.14 (0.07-0.21)	<0.001	0.14 (0.06-0.23)	0.001	-0.73 (-0.84 - -0.63)	<0.001	-0.46 (-0.57 - -0.35)	<0.001
Unspecified functional psychosis	1.27 (1.15-1.39)	<0.001	-0.01 (-0.21-0.18)	0.904	0.13 (-0.01-0.28)	0.063	-0.15 (-0.32-0.02)	0.075	-0.99 (-1.20 - -0.78)	<0.001	0.04 (-0.18 - 0.26)	0.716
Age at onset	0.03 (0.02-0.03)	<0.001	0.00 (-0.00-0.00)	0.821	0.00 (-0.00-0.00)	0.666	-0.00 (-0.01-0.00)	0.123	-0.01 (-0.01- -0.00)	<0.001	0.00 (-0.00-0.01)	0.190
Mode of onset												
Gradual vs. acute onset	0.40 (0.25-0.56)	<0.001	0.05 (-0.07-0.16)	0.407	0.03 (-0.05-0.11)	0.491	-0.03 (-0.13-0.07)	0.561	0.002 (-0.13-0.14)	0.982	0.06 (-0.09-0.20)	0.440
Insidious vs. acute onset	0.24 (0.11-0.36)	<0.001	-0.10 (-0.19- -0.01	0.037	0.17 (0.11-0.24)	<0.001	-0.07 (-0.15-0.01)	0.084	-0.03 (-0.14-0.07)	0.546	0.12 (0.003-0.23)	0.045
Premorbid work adjustment												
Poor vs. good	0.86 (0.74-0.97)	<0.001	0.11 (0.02-0.20)	0.018	0.15 (0.09-0.22)	<0.001	0.23 (0.15-0.31)	<0.001	-0.13 (-0.24 - -0.02)	0.016	-0.00 (-0.12-0.11)	0.936
Premorbid social adjustment												
Poor vs. good	0.48 (0.34-0.60)	<0.001	0.07 (-0.02-0.16)	0.144	0.08 (0.01-0.14)	0.023	0.21 (0.13-0.29)	<0.001	-0.06 (-0.17-0.04)	0.235	0.07 (-0.04-0.18)	0.198

†OPCRIT sum scores were weighted using the sign of factor loadings in the bifactor model (see table 2) as (simplified) weights to account for negative factor loadings on general and positive symptom dimensions (i.e., an item with a negative factor loading was subtracted, not added). Associations for latent factor scores of the general and specific positive symptom dimension (for which negative factor loadings were found in the bifactor model; see table 2) were markedly attenuated when using unweighted OPCRIT sum scores (general, r=0.67, 95% CI 0.64 to 0.71, p<0.001; positive symptoms, r=0.46, 95% CI 0.41 to 0.50, p<0.001).

‡ Using bipolar disorder/mania as reference category

Figure 1. Symptom profiles for general and specific psychosis dimensions by diagnosis (for publication in print)†



† **Explanatory Note:** Symptom profiles are the mean factor scores for 1 general psychosis dimension and 5 specific psychosis dimensions (positive symptoms, negative symptoms, disorganization, mania, depression) by diagnostic categories (schizophrenia, schizoaffective disorder, hypomania, and bipolar disorder/mania). Factor scores are standardized with mean = 0 and SD=1. Given negative factor loadings were found for mania items on the general psychosis dimension, patients with low ratings on all OPCRIT items are assigned a factor score close to the mean=0, whereas patients with high ratings on mania items but low ratings on other psychotic symptoms are assigned a negative factor score and patients with low ratings on mania items but high ratings on other psychotic symptoms are assigned a positive factor score. Symptom profiles showed high (positive) mean scores for schizophrenia on the general psychosis dimension as well as on the specific positive, negative, and disorganized symptom dimension, but low (negative) mean scores on the specific manic and depressive symptom dimension. There were also high (positive) mean scores on the general psychosis and specific positive, negative, and disorganized symptom dimension for schizoaffective disorder. However, on the specific manic symptom dimension, mean scores for schizoaffective disorders were higher than for schizophrenia and comparable to the mean scores of bipolar disorder/mania. Mean scores on the specific depressive symptom dimension were higher in schizoaffective disorder than in all other diagnostic categories. Low (negative) mean scores were found for bipolar disorder/mania and hypomania on the general psychosis dimension as well as on the specific positive, negative, disorganized, and depressive symptom dimension. However, compared with other diagnostic categories, mean scores were significantly higher on the specific mania dimension for these diagnoses.

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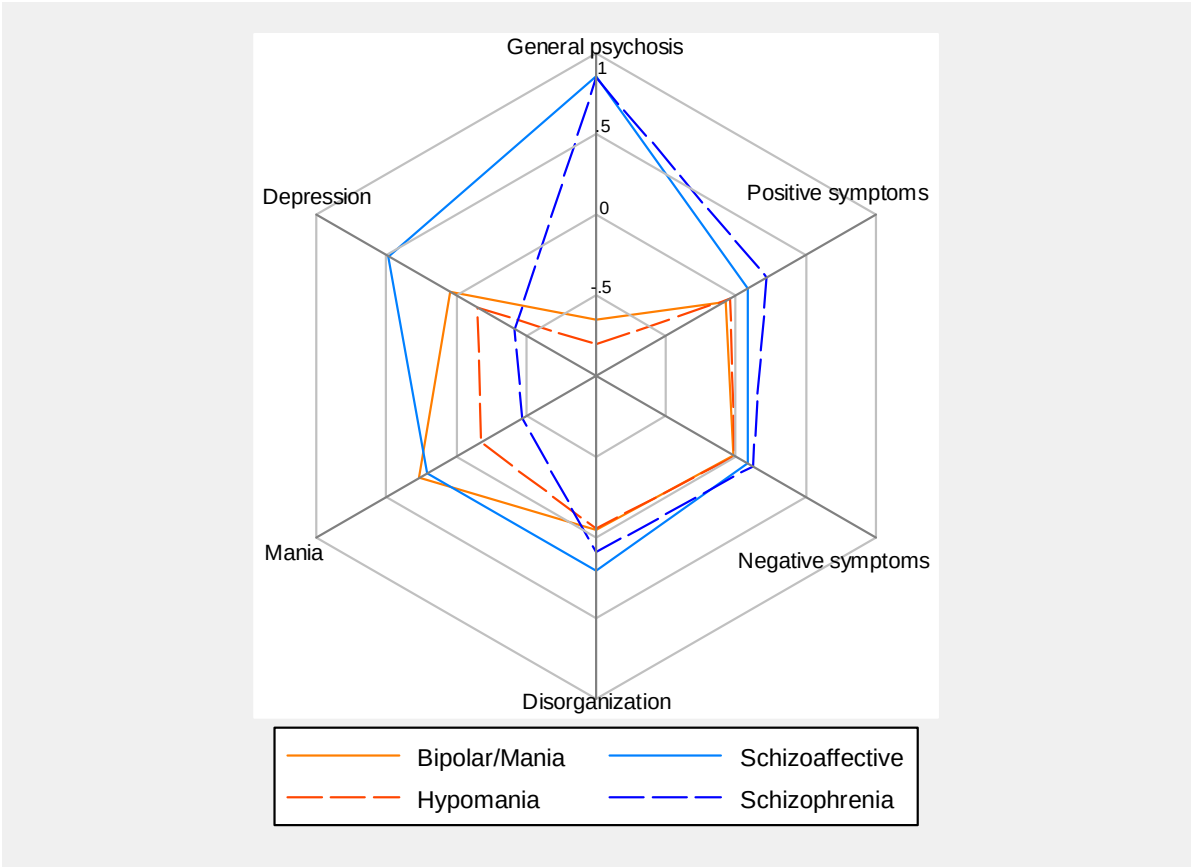

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