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The Common Structure of the Major Psychoses: More Similarities Than Differences in the Network Structures of Schizophrenia, Schizoaffective Disorder, and Psychotic Bipolar Disorder

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***Background and Hypothesis*: There has been a century-long debate about whether the major psychoses (eg, bipolar disorder, schizophrenia, and schizoaffective disorder) are one disorder with various manifestations or different disease entities. Traditional approaches using dimensional models have not provided decisive findings. Here, we address this question by examining the network constellation of affective and psychotic syndromes. *Design*: Comparable symptom data of 1882 patients with psychotic bipolar disorder, schizoaffective disorders, and schizophrenia were extracted from three datasets: B-SNIP 1, B-SNIP2, and PARDIP. Twenty-six items from the Positive and Negative Syndrome Scale, YMRS, and the Montgomery-Asberg Depression Rating Scale were selected for the analysis using a principled approach to eliminate overlapping/redundant items. Gaussian graphical models were estimated and assessed for stability, and their communities were identified using bootstrapped exploratory graph analysis. The structures and global densities of the networks were compared with network comparison tests. *Results*: The network structures were highly similar ($r >. 80$) across diagnostic groups. For all diagnoses, manic symptoms were more connected with positive symptoms while depressive symptoms were more linked with negative symptoms. The depressive and negative symptoms were the strongest indicators of depressive and psychotic communities. Theoretically interesting variability in network edge weights between symptoms was found relating to thought disorder and pessimistic thinking. *Conclusions*: The same broad structure of psychopathology underlies the symptom expressions of bipolar disorder, schizoaffective disorder, and schizophrenia. Future studies should build on the present finding by comparing specific inter-relations between symptoms in the different diagnostic groups using methods capable of detecting causality.**

Key words: bipolar/schizoaffective/schizophrenia/network/psychopathology

Introduction

Bipolar disorder and schizophrenia often lead to lasting disabilities, with the former characterized by severe mood dysregulations, while psychotic symptoms are prominent in schizophrenia.[1] Although these diagnostic constructs have been employed since the late 19th century,[2] it has long been debated whether the major psychoses are different disorders, one entity with different manifestations,[3–5] or whether there is a schizophrenia-bipolar spectrum with schizoaffective disorder as an intermediate phenotype.[6,7]

There are many similarities between the two diagnoses. Bipolar patients often experience positive symptoms,[8] while affective symptoms are common in schizophrenia patients.[9] Genetic and familial commonalities such as shared genome loci have been identified,[10] and the disorders are mutually heritable.[11] They also share environmental risk factors such as stress and trauma.[12]

In the last two decades, new approaches have emerged to understand the complexities of psychiatric disorders. Dimensional approaches, based on latent variable statistical principles, consider mental disorders as complex entities composed of different psychopathological dimensions with varying severities[13] and, compared to categorical classifications, have the advantage of not losing clinical information.[14] They have been extended to

higher-order and bifactor models that can accommodate multiple levels of classification. For example, it has been argued that models with both a general psychosis factor and separate factors corresponding to symptom dimensions are a better explanation of symptom covariation than models that include symptom dimensions alone.[15–17] This kind of approach finds its ultimate expression in the Hierarchical Taxonomy of Psychopathology under development by researchers in the United States.[18]

An alternative network approach to understanding the structure of psychopathology does not assume that the covariation between symptoms necessarily reflects underlying latent disease entities. Instead, psychiatric disorders are conceptualized as complex systems determined by causal relationships between symptoms.[19] Communities of highly interconnected symptoms can be determined, and symptoms that are most central in terms of their connectivity to other symptoms can be identified and may have particular significance as targets for treatment.[20] From a taxometric perspective, the evidence of the continuum across different mental disorders can be obtained by observing the correlation patterns among a set of symptoms.[21] Network analysis is capable of comparing these patterns among different diagnostic groups, offering new insight into the heterogeneity of severe mental illness.[22] If different diagnoses within the psychosis spectrum reflect different disease entities, we would not expect their network structures to be the same, but if they are different expressions of the same underlying disease processes, the network structure should be very similar although symptom expression is different. Hence, in this paper, we test the hypothesis that bipolar disorder, schizoaffective disorder, and schizophrenia are different manifestations of the same underlying psychopathology by comparing their network structures.

Only two studies have previously reported comparisons of this kind. Peralta et al[23,24] evaluated the network structure of symptoms assessed using the Comprehensive Assessment of Symptoms and History comparing patients with major psychoses (SCZ, $n = 908$) and affective psychoses ($n = 590$)[23] on 73 symptoms, and then schizoaffective disorder (SCA, $n = 124$) and psychotic bipolar disorder (PBD, $n = 345$)[24] on 28 symptoms, finding diagnostic groups differed in network structure in each comparison. However, neither directly compared schizophrenia and bipolar patients, and a check for conceptual similarities among nodes (items) was not employed, which is an important limitation since the robustness of network findings can be undermined by redundant items. Consequently, the comparability of schizophrenia and bipolar disorder network structures has yet to be established.

Therefore, we aimed to use network analysis to test the hypothesis that diagnoses across the psychosis spectrum have similar structures consistent with them being different manifestations of the same psychopathological processes. We constructed symptom networks for a broad sample of patients with psychosis and then for the three different groupings, SCZ, PBD, and SCA, comparing their network structures, the composition of communities, and the connectivities between specific symptoms.

Methods

Sample Selection

The current study used secondary data extracted from three studies: Bipolar and Schizophrenia Consortium for Parsing Intermediate Phenotypes (B-SNIP 1), B-SNIP2, and Psychosis and Affective Research Domains and Intermediate Phenotypes (PARDIP).[25–27] These studies used the same instruments and methodology to examine the manifestations of psychosis comprehensively in populations diagnosed with bipolar disorder, schizoaffective disorder, and schizophrenia. The datasets were obtained from the US National Institute of Health archive (https://nda.nih.gov/), and we are grateful to the original researchers on these projects for making the data available in this way.

The combined dataset included assessments of 1882 patients who were clinically stable and not in acute symptomatic states. The mean age was 37.76 years ($SD = 12.30$ years). In total, 927 patients were male and 955 patients were female. A total of 559 had a diagnosis of PBD or bipolar patients with psychotic features (ie, delusions or hallucinations). In total, 542 had a diagnosis of schizoaffective disorder (SCA) and 687 had a diagnosis of schizophrenia (SCZ). All diagnoses were made by trained clinicians who used the Structured Clinical Interview for DSM-IV Axis I Disorders, SCID-I.[28] Symptoms were assessed by the expert clinicians using the assessment tools described below. Table 1 details demographic and clinical information of the patients.

Assessment Tools and Variable Selection

The Structured Clinical Interview for the Positive and Negative Syndrome Scale (PANSS) was used to assess positive and negative psychotic symptoms and symptoms of general psychopathology.[29] It contains 30 items and the rating score for each item ranges between 1 (ie, absent) and 7 (ie, extreme). This tool is considered gold standard for psychiatric evaluations.[30] Manic symptoms were evaluated with the Young Mania Rating Scale (YMRS), which are widely applied in clinical settings.[31] This measure contains 11 items and the rating score for each ranges either from 0 to 4 or 0 to 8. For example, elevated mood is rated from 0 (ie, absent) to 4 (ie, euphoria), and disruptive—aggressive behavior is rated from 0 (ie, absent) to 8 (ie, assaultive). Depressive symptoms were assessed using the Montgomery-Asberg Depression Rating Scale (MADRS), and its validity and sensitivity were supported by prior studies.[32,33] The MADRS contains 10

Table 1. Demographic and Clinical Information of Full Sample

	Sample		
Sources			
B-SNIP1, *n* (%)	834 (43.12)		
B-SNIP2, *n* (%)	922 (47.67)		
PARDIP, *n* (%)	178 (9.20)		
Total *n* (%)	1934 (100)		
Valid *n* (%)[a]	1882 (97.31)		
Age, *M* (*SD*)	37.76 (12.30)		
Gender			
Female, *n* (%)	955 (50.74)		
Male, *n* (%)	927 (49.26)		
Race[b], *n* (%)			
American Indian/Alaska Native	4 (0.37)		
Asian	25 (2.33)		
Black or African American	426 (39.63)		
White	565 (52.56)		
More than one race	55 (5.12)		
Marital status[c], *n* (%)			
Divorced/separated	190 (17.12)		
Never married/ single	719 (64.77)		
Presently married or in a sustained conjugal relationship	183 (16.49)		
Widowed	18 (1.62%)		
Diagnoses[d]	PBD	SCA	SCZ
n (%)	559 (29.70)	542 (28.80)	687 (36.50)
PANSS, *M* (*SD*)	54.41 (17.39)	66.90 (18.55)	65.18 (18.71)
Positive, *M* (*SD*)	13.06 (5.12)	17.77 (6.11)	16.82 (6.10)
Negative, *M* (*SD*)	12.27 (5.19)	15.40 (5.93)	16.70 (6.26)
General, *M* (*SD*)	29.08 (9.25)	33.74 (9.24)	31.66 (9.50)
YMRS, *M* (*SD*)	6.99 (7.73)	9.67 (7.82)	7.45 (6.71)
MADRS, *M* (*SD*)	11.82 (10.59)	14.31 (10.40)	8.67 (8.57)
In receipt of medications, Y/N (%)[e]	233/15 (93.95/6.05)	218/9 (96.04/3.96)	246/9 (96.47/3.53)
Age of first hospitalization, *M* (*SD*)[f]	25.43 (9.86)	22.70 (9.14)	22.74 (7.46)
Number of hospitalizations, *M* (*SD*)[g]	5.30 (6.20)	6.91 (7.33)	5.91 (6.72)
Age of first psychotic episode, *M* (*SD*)[h]	22.27 (9.59)	18.76 (8.99)	20.85 (7.80)

Note: MADRS, Montgomery-Asberg Depression Rating Scale; PANSS, Positive and Negative Syndrome Scale; PBD, psychotic bipolar disorder; SCA, schizoaffective disorder; SCZ, schizophrenia; YMRS, Young Mania Rating Scale.
[a]Forty-six participants were excluded due to incomplete assessment on interested variables. Additionally, six participants were relatives of the probands and thus excluded from further analysis.
[b]The information was incomplete or missing in *n* = 807 participants.
[c]The information was incomplete or missing in *n* = 772 participants.
[d]Incomplete responses to relevant variables were distributed as follows: PBD (*n* = 13), SCA (*n* = 9), and SCZ (*n* = 24).
[e]The information was incomplete or missing in 311 PBD, 315 SCA, and 432 SCZ patients.
[f]The information was incomplete or missing in 329 PBD, 344 SCA, and 456 SCZ patients.
[g]The information was incomplete or missing in 339 PBD, 358 SCA, and 478 SCZ patients.
[h]The information was incomplete or missing in 315 PBD, 325 SCA, and 440 SCZ patients.

items, with rating scores ranging from 0 to 6, with the higher score reflecting a more severe condition.

Pilot work indicated that item redundancy (eg, between almost identical items P7 in the PANSS and Y9 in YMRS) created considerable distortions in the network structures. Variable selection was therefore conducted in two stages. First, face validity of all variables was evaluated by the research team and items P1 (ie, delusion) and P7 (ie, hostility), and general psychiatric symptoms from PANSS and M1 (ie, apparent sadness) from MADRS were excluded due to obvious duplication with other items. The conceptual similarities between the remaining items were determined by the weighted topological overlap (wTO) score; pairs of variables were considered conceptually similar if the score was higher than 0.25 and variables were merged by addition if they met this criterion.[34] Twenty-six symptom variables were selected for the current analysis. The detailed variable selection procedure and the rationale for specific decisions can be found in Supplementary table 1. As a sensitivity test, we repeated all analyses using item selection guided solely by wTO scores (ie, without first reducing items that, on

face validity, seemed to overlap; see Supplementary table 1b). This made no substantial difference to the results. For example, correlations of networks across different diagnostic groups using items entirely determined by the wTO scores were, in all cases, > .85, which did not differ from the original findings.

Statistical Analyses

All computations were conducted using R studio (version 2023.06.0) with R language (version 4.3.1) as the backend. The Kruskal–Wallis rank-sum test was used to compare the symptom ratings across multiple groups, and the pair-wise Wilcoxon test was subsequently used to show the results of group-to-group level comparisons with the *P* value adjusted by the BH (Benjamini and Hochberg) method.[35] The effect sizes (*r*) for these tests were similarly reported, with a range between (.10 to .29) indicating a small effect size, (.30 to .49) representing a moderate effect size, and values higher than .50 considered as a large effect size. The *bootnet* package (version 1.5.6) was utilized to estimate networks and evaluate the network stabilities. The *qgraph* package (version 1.9.5) was used to compute the centralities and draw relevant graphs. The *igraph* package (version 1.5.1) was used to compute the network statistics (eg, density). The network communities and the stabilities were computed using the *EGAnet* package (version 2.02); the *wTO* scores were computed using this package via the function *UVA* (Unique Variable Analysis).[36] *NetworkComparisonTest* (version 2.2.2) was used to compare networks.

Network Estimation

The network structures for the total patient population and subgroups with different diagnoses were estimated by graphic lasso based on extended BIC criterium (EBICglasso), with a default hyperparameter value (γ = .5) for regularized networks.[19] No skip structure was involved during the assessment. Spearman correlation/rank transformations were taken as inputs owing to the skewed distributions of the ratings.[37] Three node centralities were calculated: strength (ie, how strongly a node is connected to other nodes), closeness (ie, the degree a node is indirectly connected to other nodes), and betweenness (ie, the degree to which a node acts a mediator connecting two other nodes in the network). Network stability was assessed by nonparametric bootstrapping with 3000 iterations.[19] The stability of node statistics was reflected by the correlation stability (CS) coefficient, with a range between 0 and 0.75. For example, a CS coefficient value of 0.75 indicates that a correlation value of 0.70 in at least 95% of the samples can be attained with 75% of the sample dropped. A fairly robust node statistic is indicated by a CS coefficient value larger than 0.50. The stability of edges can be evaluated by visual inspection of the confidence interval (CI) plot, such that a wider CI suggests less stable edge statistics.

The network communities were computed via exploratory graphic analysis (EGA), which is a network method comparable to exploratory factor analysis.[34] As for the network estimations, Spearman correlations were used as inputs in the EGA. The Walkstrap algorithm was used to find densely connected subgroups among all variables.[38] The empirical structures for all patients and subgroups were plotted. The Total Entropy Fit Index (TEFI) reflects the accuracy of the structure, with lower values indicating better structural fit. The structural consistency and item stability were evaluated by 1000 nonparametric iterations; the structural consistency represents the proportion of replicated item compositions in bootstrapped samples, while item stability reflects the proportion of times a node was placed in a specific dimension.

Network Comparison

The network comparison test (NCT) was used to examine group differences.[39] Specifically, the invariance of global strength and invariance of network structure (ie, omnibus test) tests were conducted to compare the global connectedness and the differences in edges by groups with different diagnoses. For illustration, the density (ie, the number of edges with non-zero weights/the total number of edges) and the MAEW (mean absolute edge weights) of the network were also reported. A post hoc test with BH adjustment was run when the omnibus test was significant. The NCT was computed based on 2000 iterations.

Results

Comparisons of Symptoms Between Diagnostic Groups

Significant differences were observed in all symptoms across groups except for Y10 (Appearance; YMRS). The PBD patients had lowest severity for all psychotic symptoms, except for P4 (Excitement; PANSS). In addition, the SCA patients reported generally higher severity of positive psychotic symptoms, while the SCZ patients had generally higher severity of negative psychotic symptoms. The SCA and PBD patients had comparable severity on most manic symptoms, and their symptom scores were both higher than those of SCZ patients. However, the pattern was different for Y7 (Thought disorder; YMRS) and Y11 (Insight; YMRS). The SCA patients reported the most severe thought disorders compared to both SCZ and PBD patients, while the SCZ patients exhibited the poorest insight, followed by SCA and PBD patients. Severities of the most depressive symptoms were ranked in subgroups as follows: SCA > PBD > SCZ. Nonetheless, the serveries of M5 (Reduced appetite; MADRS), M6 (Concentration difficulty; MADRS), and SP (Sleep problems; YMRS and MADRS) did not follow this order. Most of the comparisons exhibited

small effect sizes, although some psychotic symptoms, such as hallucinations, showed moderate effect sizes; see Supplementary table 2 for details.

Network Structure for the Total Psychotic Population

The network structure in the full sample was very stable; see figure 1. All node centralities (ie, strength, closeness, and betweenness) exhibited high robustness (CS coefficient = 0.75), and the edge weights CIs were fairly narrow; see Supplementary figure 1a for details.

The density of the network was 0.51, and the absolute average mean weight was 0.036. WD (Withdrawal; PANSS) was a bridge symptom linking depressive (eg, M8, Inability to feel; MADRS) to positive symptoms (eg, P6, Suspiciousness; PANSS). Perhaps not surprisingly, P4 (Excitement; PANSS) was the node that linked most clearly to manic symptoms such as ME (Elevated mood; YMRS) and to other positive symptoms (eg, P5: Grandiosity). Manic symptoms were more connected to positive psychotic symptoms while depressive symptoms were more linked to negative psychotic symptoms. The edge with highest weight was N1 (Blunt affect: PANSS)-RC (Poor rapport and rigid conversation; PANSS) ($W = 0.41$, 95% BCI: 0.37–0.46), whereas the lowest weight was observed on edge N7 (Stereotyped thinking; PANSS)-IA (Irritability/disruptive and aggressive behavior; YMRS) ($W = 0.001$, 95% BCI: −0.02 to 0.02). A full list of all non-zero edges and their statistics can be found in Supplementary table 3a. The node with highest strength in this network was M3 (Inner tension; MADRS), and Y11 (Insight; YMRS) was the node with the lowest strength; the nodes with highest level of betweenness and closeness were M8 (Inability to feel; MADRS) and WD (Withdrawal; PANSS); see figure 2 and Supplementary figure 2 for details.

Network Structures in Specific Diagnostic Groups

PBD Network. The edge statistics of the PBD network were fairly stable; see Supplementary figure 1b for details. The node statistics were stable for strength (CS coefficient = 0.67), but less stable for closeness (CS coefficient = 0.44) and betweenness (CS coefficient = 0.28), meaning that these statistics should be interpreted with caution.

A visualization of the PBD network can be seen in figure 1. Positive psychotic symptoms (eg, P4: Excitement, P6: Suspiciousness/persecution; PANSS) were mostly linked with manic symptoms (eg, Y6: Speed and amount of speech, IA: Irritability/disruptive and aggressive behavior; YMRS), while negative psychotic symptoms (eg, WD: Withdrawal; PANSS) were mostly connected with depressive symptoms (eg, M8: Inability to feel; MADRS). The strongest edge in this network was the same as that of general population but with lower weights ($W = 0.38$, 95% BCI: 0.31–0.47), while the edge with lowest weights was P6 (Suspiciousness/persecution; PANSS)–M6 (Concentration difficulties; MADRS) ($W = 0.001$, 95% BCI: −0.03 to 0.04). The complete list can be found in Supplementary table 3b. The node with highest degree of strength in this network was M8 (Inability to feel; MADRS), while the node with lowest strength in the network was Y11 (Insight; YMRS); see figure 2.

SCA Network. The network of SCA patients, shown in figure 1, was stable in terms of node strength (CS coefficient = 0.59) and edge weights (see Supplementary figure 1c), but the stabilities of closeness and betweenness were low (CS coefficient = 0.28). The pattern of connections was similar to that seen in the PBD patients. The strongest edge in the network was N1 (Blunt affect; PANSS)–RC (Poor rapport and rigid conversation; PANSS) ($W = 0.39$, 95% BCI: 0.29–0.44), while the smallest edge was P6 (Suspiciousness/persecution; PANSS)–M5 (Reduced appetite; MADRS) ($W = 0.001$, 95% BCI: −0.03 to 0.04); see a full list of the edge statistics in Supplementary table 3c. The node with highest strength within this network was WD (Withdrawal; PANSS), while the node with lowest degree of strength was Y11 (Insight; YMRS); see details in figure 2.

SCZ Network. The network of SCZ exhibited good stabilities for node strength (CS coefficient = 0.59) and node closeness (CS coefficient = 0.52), and moderate stability for betweenness (CS coefficient = 0.44). The edges were fairly stable (see Supplementary figure 1d).

The network pattern in SCZ patients is generally similar to the other networks. Nonetheless, a significant difference was observed in the relationship between Y7 (Thought disorder; YMRS) and P2 (Conceptual disorganization; PANSS) (see figure 2). N1 (Blunt affect; PANSS)–RC (Poor rapport and rigid conversation; PANSS) ($W = 0.36$, 95% BCI: 0.29–0.42) was the edge with highest weight in this network, and the edge with the lowest weight was M5 (Reduced appetite; MADRS)–M9 (Pessimistic thoughts; MADRS) ($W = 0.001$, 95% BCI: −0.04 to 0.05); see Supplementary table 3d for the full edge list. In this network, the node with highest strength was M3 (Inner tension; MADRS), while the node with lowest strength was Y11 (Insight; YMRS); the node with the highest level of betweenness was Y7 (Thought disorder) (see figure 2).

Network Communities

The number of communities ranged from 3 for the general sample and the PBD group to 6 for the SCZ group. This variation reflected some symptoms that were not stably attributed to communities in some analyses. Most notably, P3 (Hallucinations, PANSS) and P6 (Suspiciousness, PANSS) appear with other psychotic

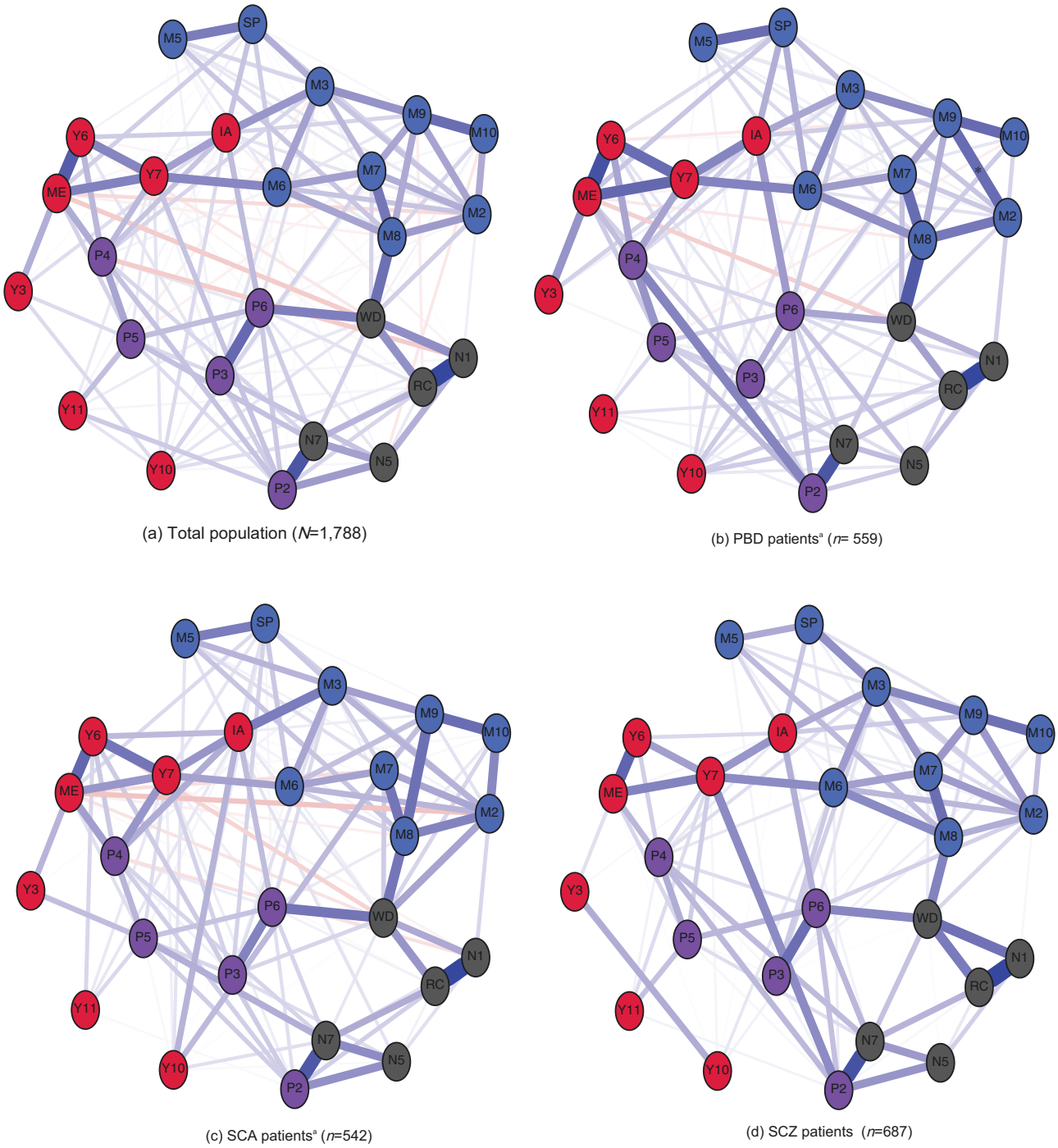

Fig. 1. Network structure of selected variables in general and psychotic patients. The node colors were scale determined. *Positive symptoms*: P2 (Conceptual disorganization), P3 (Hallucinations), P4 (Excitement), P5 (Grandiosity), P6 (Paranoia/suspiciousness); *Negative symptoms*: N1 (Blunt affect), RC (Poor rapport and rigid conversation), WD (withdrawal), N5 (difficulty in abstract thinking), N7 (Stereotyped thinking); *Manic symptoms*: ME (Mood/energy elevation), IA (Irritability/aggressive-disruptive behavior), Y3 (Sexual interests), Y6 (Speed and amount of speech), Y7 (Language thought disorder), Y10 (Appearance), Y11 (Insight); *Depressive symptoms*: M2 (Reported sadness), M3 (Inner tension), M5 (Reduced appetite), M6 (Concentration difficulty), M7 (Retardation), M8 (Inability to feel), M9 (Pessimistic thoughts), M10 (Suicidal thoughts), SP (Sleep problems). The blue edges represent positive correlations between nodes, and the red edges represent negative correlations. The color for nodes was predefined by questionnaires. $^{*}P < .05$, $^{**}P < .01$, $^{***}P < .001$. [a]The overall centrality ($S0$) and maximum edge difference (M) across compared subgroups were PBD and SCZ ($S0 = 2.20^{***}$, $M = .13$), SCA and SCZ ($S0 = 2.07^{*}$, $M = .17$), and PBD and SCA ($S0 = .18$, $M = .13$). *Theoretically interesting edge differences: P2–Y7 (SCZ > PBD*/SCA**), M8–M9 (SCA > SCZ**), M2–M9 (PBD > SCA**).

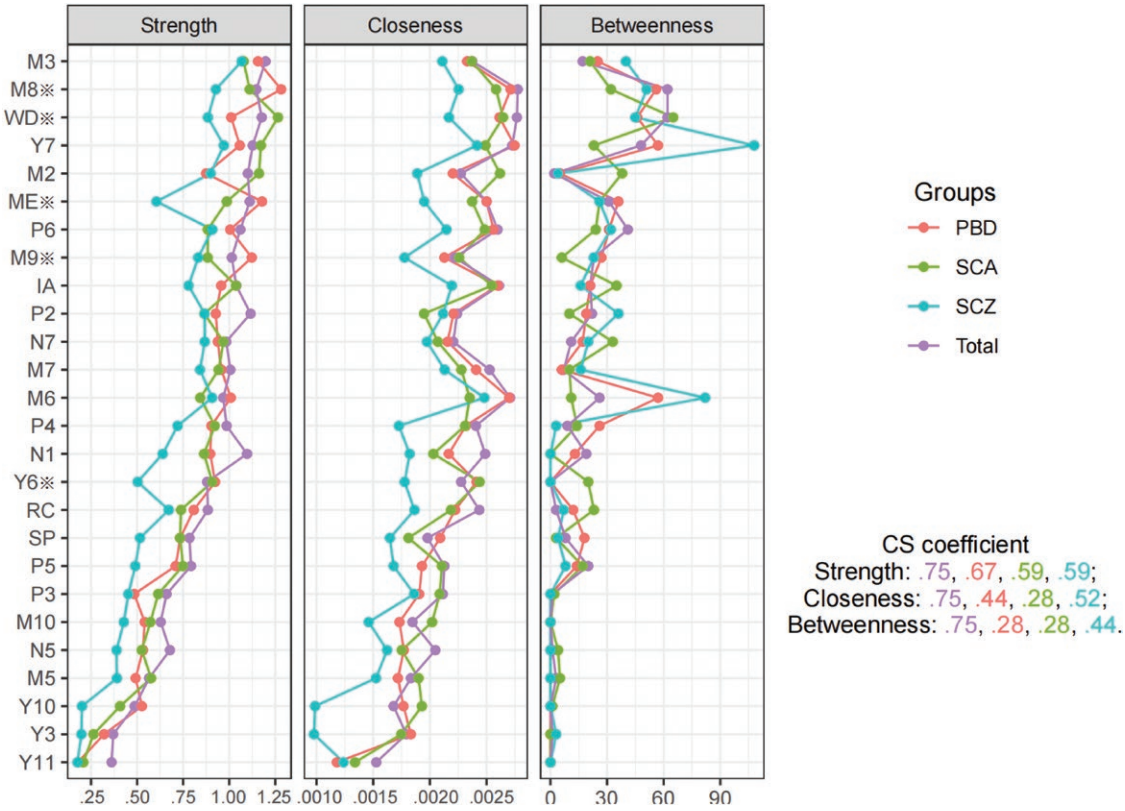

Fig. 2. Node centralities of the estimated network models. *Positive symptoms*: P2 (Conceptual disorganization), P3 (Hallucinations), P4 (Excitement), P5 (Grandiosity), P6 (Paranoia/suspiciousness); *Negative symptoms*: N1 (blunt affect), RC (poor rapport and rigid conversation), WD (withdrawal), N5 (difficulty in abstract thinking), N7 (stereotyped thinking); *Manic symptoms*: ME (Mood/energy elevation), IA (Irritability/aggressive-disruptive behavior), Y3 (Sexual interests), Y6 (Speed and amount of speech), Y7 (Language thought disorder), Y10 (Appearance), Y11 (Insight); *Depressive symptoms*: M2 (Reported sadness), M3 (Inner tension), M5 (Reduced appetite), M6 (Concentration difficulty), M7 (Retardation), M8 (Inability to feel), M9 (Pessimistic thoughts), M10 (Suicidal thoughts), SP (Sleep problems). The scale used in this graph was the raw values of coefficients; $*P < .05$, $**P < .01$. ※Node strength statistics with adjusted P values: PBD > SCZ (ME**, Y6**, M8**, M9*), SCA > SCZ (WD**, Y6*).

symptoms in the general and PBD samples but are not consistently attributed to a community in the SCA and SCZ samples. Across the bootstrapped analyses, the most replicable community consisted of all the depressive symptoms; for most of the groups, the structural consistency was higher than 75% and the node replicability was higher than 95%, indicating that the composition of this community was very stable. The communities with lowest stabilities comprised psychotic symptoms and manic symptoms; interestingly, the most stable nodes in the psychosis community were negative symptoms and conceptual disorganization. See figure 3 and Supplementary table 3 for further details.

Network Comparisons by Diagnostic Groups

Densities of the networks of PBD, SCA, and SCZ were 0.43, 0.42, and 0.35, respectively; the MAEWs (mean absolute edge weights) were 0.033, 0.033, and 0.022, respectively. See Supplementary figure 3a for the distribution of the weighted network densities. The networks for PBD ($S_0 = 2.20$, $P < .001$) and SCA ($S_0 = 2.07$, $P = .02$) patients had a higher global connectivity than that for SCZ patients, but the difference between SCA and PBD patients was not significant ($S_0 = 0.12$, $P = .81$). Omnibus test revealed non-significant differences between network structures of PBD and SCZ ($M = 0.13$, $P = .47$), SCA and SCZ ($M = 0.17$, $P = .06$), and between those for PBD and SCA ($M = 0.18$, $P = .07$). Similarly, the weight matrixes of the edges were highly correlated across all compared networks: PBD and SCA ($r = .85$), PBD and SCZ ($r = .85$), and SCA and SCZ ($r = .83$).

Regardless of the non-significant findings yielded by omnibus tests, an exploratory inspection of the edge variability network plotted in Supplementary figure 4 suggested that the edges P2 (Conceptual disorganization; PANSS)–Y7 (Thought disorder; YMRS), M2 (Reported sadness; MADRS)–M9 (Pessimistic thoughts; MADRS), and M8 (Inability to feel; MADRS)–M9 (Pessimistic thoughts; MADRS) exhibited high variabilities in weights across different networks; these edges are theoretically interesting for reasons detailed in "Discussion"

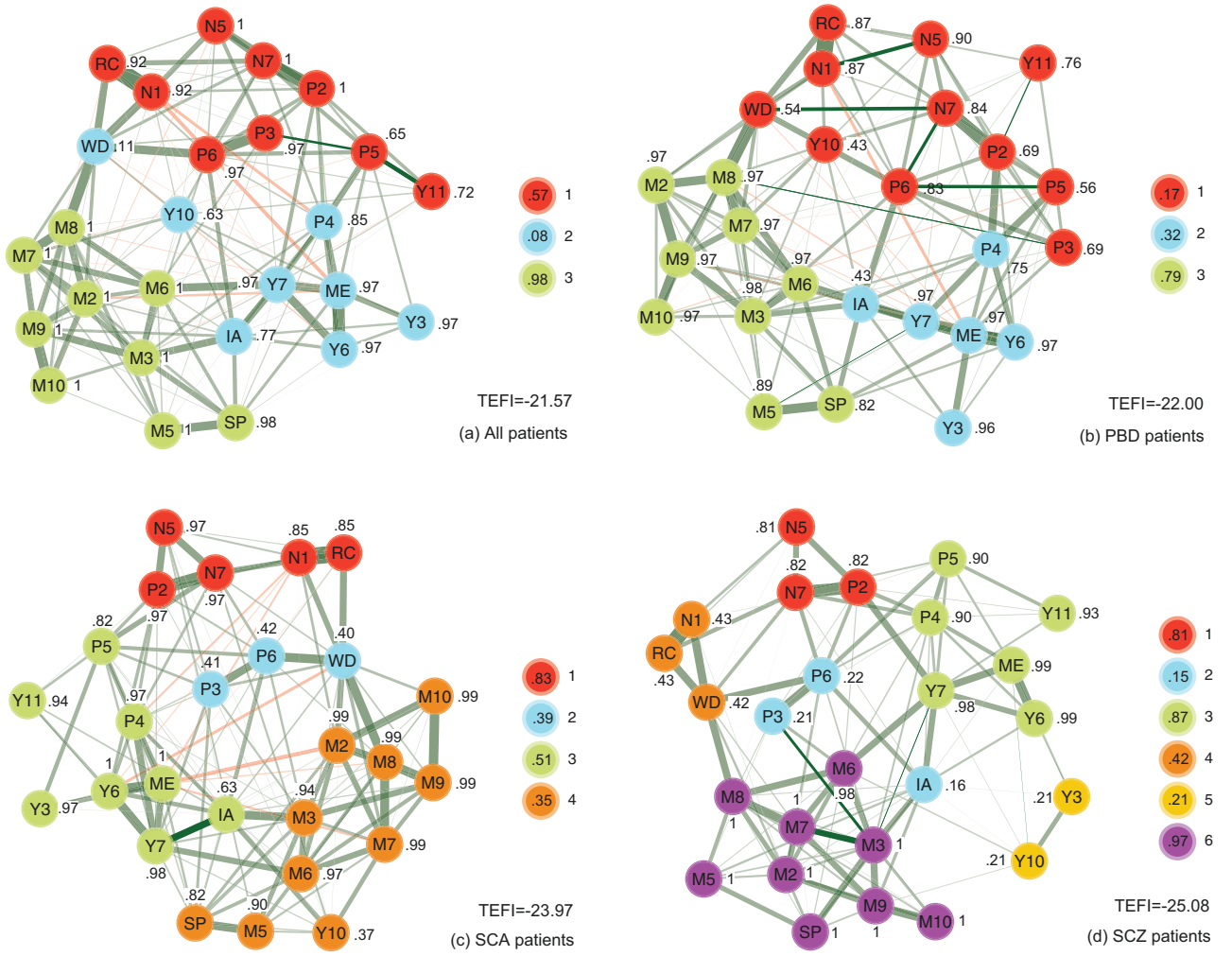

Fig. 3. The empirical network communities of affective and psychotic syndromes in all patients and subgroups. *Psychotic symptoms*: P2 (Conceptual disorganization), P3 (Hallucinations), P4 (Excitement), P5 (Grandiosity), P6 (Paranoia/suspiciousness), N1 (blunt affect), RC (poor rapport and rigid conversation), WD (withdrawal), N5 (difficulty in abstract thinking), N7 (stereotyped thinking); *Manic symptoms*: ME (Mood/energy elevation), IA (Irritability/aggressive-disruptive behavior), Y3 (Sexual interests), Y6 (Speed and amount of speech), Y7 (Language thought disorder), Y10 (Appearance), Y11 (Insight); *Depressive symptoms*: M2 (Reported sadness), M3 (Inner tension), M5 (Reduced appetite), M6 (Concentration difficulty), M7 (Retardation), M8 (Inability to feel), M9 (Pessimistic thoughts), M10 (Suicidal thoughts), SP (Sleep problems); The coloring of the nodes and dimensions was determined empirically. Each node is accompanied by a number indicating its stability to the corresponding dimension. The color and number representing each dimension are displayed on the right side of the graph of communities; the number within each node indicates the structural consistency of the dimension. The Total Entropy Fit Index (TFEI) is presented in the right bottom of each graph of communities, with lower values suggesting a more accurate structure.

section. Therefore, post hoc analyses were conducted to compare the three edges across networks. The permutation test showed that edge weights of P2–Y7 were higher in SCZ patients than that of SCA ($E = .13$, $P_{adjusted} < .01$) and PBD ($E = .13$, $P_{adjusted} = .02$) patients. The weights of M2–M9 were lower in the SCA network than the PBD network ($E = .18$, $P_{adjusted} < .01$), and the weights of M8–M9 were lower in the SCZ network than SCA network ($E = .17$, $P_{adjusted} < .01$). The weights of the two edges between depressive symptoms were not statistically different between networks of SCZ and PBD patients. See table 2 and Supplementary figure 3b for details.

Discussion

The current analysis examined the network structures of affective and psychotic syndromes in patients diagnosed with schizophrenia, schizoaffective disorder, or PBD. The data were drawn from three high-quality studies with large, representative samples using gold-standard psychiatric assessments conducted by trained clinicians. We used a principled approach to item selection which eliminated redundancy that might otherwise have distorted the findings. Our findings are consistent with the work of Peralta et al[23,24] in the relationship between affective and psychotic syndromes. Specifically, the manic symptoms

Table 2. The Weights of Three Varied Edges and the Statistics Across Networks

Networks	PBD	SCA	SCZ	Direction
P2–Y7	0.03	0.03	0.16	SCZ > SCA**; SCZ > PBD*
M2–M9	0.22	0.04	0.14	PBD > SCA**
M8–M9	0.12	0.21	0.05	SCA > SCZ**

Note:
*$P < .05$,
**$P < .01$. The results were based on 2000 iterations; the P value was adjusted by the BH method.

were more linked with positive symptoms while depressive symptoms were more linked with negative symptoms. However, our findings are distinct from the previous work in the following aspects.

The first and most striking finding, which is in contrast to the studies by Peralta et al, is that, although symptom ratings differed very considerably between the three diagnostic groups, the network structures were nearly identical. Based on the definition of statistical dimensions,[21,40] this similarity would not have been expected if the three diagnoses were reflections of distinct psychopathological processes. Therefore, the findings are consistent with the hypothesis that the same underlying psychopathological processes lead to the varying symptom expressions which, according to the exact symptoms experienced, are then classified during the assessment process (and presumably by clinicians in general psychiatric practice) into the three diagnostic groups. This interpretation is consistent with recent attempts to create new taxonomic models that emphasize the hierarchical nature of disorders (with conventional diagnoses contained within higher-order classifications) such as the three spectra (internalizing, externalizing, and reality-impairing) model[41] and the HiTOP approach.[18]

Examination of the individual symptom differences helps clarify this picture. As would be expected, the PBD patients had lowest severity for all psychotic symptoms, except for excitement. However, unexpectedly perhaps, SCA patients reported the most severe positive psychotic symptoms while, expectedly, the SCZ patients had more severe negative symptoms. The SCA and PBD patients were comparable in the severity of most manic symptoms, which were more severe than those observed in SCZ patients.

Examination of the community structures provides further insights that help us to interpret these findings. Although there was inconsistency between the groups, in both the analysis of the sample as a whole and across the diagnoses, depressive and negative symptoms showed the greatest replicability. Positive and manic symptoms, by contrast, were unstable and fluctuated in their placement across communities. In as much as core psychopathological symptoms are likely to lead to stable communities, these findings could suggest that depressive and negative symptom processes are primary drivers of severe mental illness, with positive and manic symptoms possibly being a reaction to them. The node centralities revealed a similar story, as the nodes with highest strength were either depressive (eg, Inability to feel) or negative symptoms (eg, Withdrawal) across the subgroups. This interpretation would be consistent with some foundational accounts of severe mental illness. For example, in contrast to the post-DSM-III focus on positive symptoms, Kraepelin[2] highlighted negative symptoms as the primary feature of dementia praecox/schizophrenia, and Bleuler argued that the positive symptoms are reactions to fundamental disturbances that included disordered associations, affect, ambivalence, together with autism (conceived of as a flight into a preferred reality); a similar view has been taken by more recent phenomenological researchers.[42] Similarly, Karl Abraham argued that manic symptoms are a reaction to underlying depressive processes and this hypothesis has some support from more recent psychopathological investigations.[20,43–45] A possible objection to this interpretation is that it seems inconsistent with the observation that positive symptoms cause great distress and often provoke greatest clinical concern. However, there is evidence that distress in psychosis is more associated with depression and low self-esteem than either positive or negative symptoms[46] and, in any case, there is no reason to assume that the most distressing symptoms are those that are most central to the disease process (by analogy, in many medical conditions, pain is the main source of distress but is not the central pathological process). An implication of our admittedly speculative interpretation of our data is that advances in the treatment of psychosis might be achieved by researchers developing treatments that are more focused on negative emotions and negative symptoms.

Our exploratory analyses of differences in specific edge weights should be interpreted with caution given the results of omnibus tests and the lack of a priori hypotheses but are nonetheless of potential theoretical interest. The role of cognitive versus affective processes in thought disorder has long been debated. The Bleulerian view that loosening of association was a driving process in schizophrenia has been supported by empirical research,[47] suggesting that this process is specifically associated with thought disorder but, at the same time, there is evidence that affective reactivity plays a role in disordered speech

in both schizophrenia and bipolar disorder.[48,49] The network structure observed here suggests that both processes may be important, but the high variability in the edge between thought disorder and conceptual disorganization suggests that this latter process is more important in schizophrenia patients.

Pessimistic thought (M9) plays a role in both the highly variable edge comparisons in depressive symptoms, in relation to both *Reported sadness* (M2: MADRS) and M9 and *Inability to feel* (M8: MADRS). Learned hopelessness theory suggests that a pessimistic attributional (explanatory) style plays a central role in depressed mood,[50] and this relationship seems reflected in the network model of PBD patients but less so in that of SCA patients. However, it is possible that this is because the SCA patients had both higher pessimism and higher depressed mood than the PBD patients (see table 2). Meanwhile, the relationship between pessimistic thought and inability to feel (a bridge symptom between depressive and negative symptoms) is more evident in SCA patients than SCZ patients, which is partially in line with a prior report that the relationship was stronger in depressed adolescents than those with subthreshold depression.[51] Speculating, it is possible that pessimistic thinking plays a role in both low mood and flat affect, but that the former relationship is more evident in PBD patients whereas the latter is more evident in SCA patients. A further speculation is that the attribution style is less significant in the path toward inability to feel and negative symptoms in schizophrenia patients than in schizoaffective patients. Further research about the relationship between attribution style and both symptoms seems merited.

Limitations

The current study utilized a large sample that was representative of the broad population of patients with psychosis; the data are of high quality and a principled approach was taken to item inclusion. However, our research has the following limitations: (1) Network models assume causal relationships between nodes in the network, but the data are correlational. The link between nodes denotes the probability of joint presence, and this presence is based on cross-sectional data so that the direction of the relationship cannot be determined. Further research is required to establish the direction of influence (eg, between conceptual disorganization and thought disorder), eg, by longitudinal/ dynamic network analysis. (2) Although the general psychotic population network comprised a large sample size and was very stable, the node centralities (eg, closeness and betweenness), replicabilities, and structural consistencies were quite unstable for some subgroups and symptoms. This could be ameliorated in the future by recruiting even larger samples to more accurately assess and understand networks in diagnostic subgroups. (3) Although the scales used in current analyses were widely accepted with good validity, they may not have captured the syndromes comprehensively. (4) Our analyses did not examine the influence of external factors on psychopathology (eg, life trauma, which may have effects on specific symptoms). Future work including these factors in network analyses may be informative about the role of the environment in the course of mental illness.

A final caveat is that there is no known way of comparing network models with the longer established latent variable models, which have recently pointed to a transdiagnostic psychosis latent variable.[15,16] Indeed, one analysis[17] supporting a general psychosis dimension has used a subset (B-SNP-I) of the data used in the present analyses. Our findings of similar network structures across psychotic populations are in line with the bifactor model assumption that a general psychosis psychopathology factor is important in all diagnostic groups. However, our findings revealed 3–6 network communities within different populations, which contrasts with the factors found in the abovementioned studies using latent variable approaches. It seems plausible that both underlying latent factors and symptom-to-symptom influences are important in driving psychopathology, with exogenous factors also influencing symptom expression at both levels. However, further methodological advances are required before it will be possible to test models of such complexity.

Conclusion

The bipolar and schizoaffective disorders and schizophrenia are similar in terms of the network structure and the relationship between affective and psychotic syndromes, which is consistent with a unitary account of severe psychopathology. However, the differences in network communities and the edge weights in the networks of different diagnostic groups suggest that the underlying process generating specific symptoms may sometimes vary between groups.

Supplementary Material

Supplementary material is available at https://academic.oup.com/schizophreniabulletin/.

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