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Main Symptomatic Treatment Targets in Suspected and Early Psychosis: New Insights From Network Analysis

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The early detection and intervention in psychoses prior to their first episode are presently based on the symptomatic ultra-high-risk and the basic symptom criteria. Current models of symptom development assume that basic symptoms develop first, followed by attenuated and, finally, frank psychotic symptoms, though interrelations of these symptoms are yet unknown. Therefore, we studied for the first time their interrelations using a network approach in 460 patients of an early detection service (mean age = 26.3 y, SD = 6.4; 65% male; *n* = 203 clinical high-risk [CHR], *n* = 153 first-episode psychosis, and *n* = 104 depression). Basic, attenuated, and frank psychotic symptoms were assessed using the Schizophrenia Proneness Instrument, Adult version (SPI-A), the Structured Interview for Psychosis-Risk Syndromes (SIPS), and the Positive And Negative Syndrome Scale (PANSS). Using the *R* package *qgraph*, network analysis of the altogether 86 symptoms revealed a single dense network of highly interrelated symptoms with 5 discernible symptom subgroups. Disorganized communication was the most central symptom, followed by delusions and hallucinations. In line with current models of symptom development, the network was distinguished by symptom severity running from SPI-A via SIPS to PANSS assessments. This suggests that positive symptoms developed from cognitive and perceptual disturbances included basic symptom criteria. Possibly conveying important insight for clinical practice, central symptoms, and symptoms "bridging" the association between symptom subgroups may be regarded as the main treatment targets, in order to prevent symptomatology from spreading or increasing across the whole network.

Key words: basic symptoms/attenuated psychotic symptoms/psychopathology/symptom dimensions/schizophrenia/depression

Introduction

The early detection and intervention in psychoses prior to their first episode have become a major issue in psychosis research.[1] It has been fueled by the fact that psychoses, notably schizophrenias, commonly develop slowly, on average over several years,[2–4] and that treatment is often long delayed in first-episode psychosis (FEP) and its initial prodrome, which is associated with poor outcome.[5,6] For the early detection of clinical high risk (CHR) of psychosis, 2 main approaches are currently pursued[1,7]: (1) the ultra-high-risk (UHR) approach[8,9] and (2) the basic symptom approach[3,10,11] (supplementary etables 1–2, eText 1). One instrument for UHR assessment is the Structured Interview for Psychosis-Risk Syndromes (SIPS)[12–14] that has been modeled on the Positive And Negative Syndrome Scale (PANSS),[15] assessing the lower PANSS ranges in more detail.[16] The PANSS is the main scale for assessing frank psychotic symptoms that has also been used to detect CHR states.[16] Basic symptoms are commonly assessed with the Schizophrenia Proneness Instrument, Adult version (SPI-A).[17]

Current models of the early course of psychoses assume that basic symptoms develop first, followed by attenuated psychotic symptoms (APS) before transient (ie, BLIPS) and/or more persistent frank positive psychotic symptoms develop.[3,7,18] In line with this, cognitive basic symptoms were recently found to mediate the relationship between positive and negative schizotypy and attenuated positive and negative symptoms as assessed with the SIPS.[19] Thus, as regards models of emerging psychosis,[3,7,18] persons developing psychosis and possibly already scoring higher on schizotypy trait measures[20–22] are assumed to first score high on the state measure SPI-A; second, additionally on SIPS; and finally high on PANSS. In acute psychotic states, however, ie, when scoring high on SIPS and PANSS, SPI-A might score low because subjective insight is lost and deficits are not self-perceived as dysfunctions of one's own information processing anymore.

Dimensional analyses—predominately orthogonal factor analyses—mainly found a 5-factor structure for the PANSS in schizophrenia patients,[23,24] with 4 consistent factors such as positive, negative, disorganization, and excitement, and a fifth less consistent factor, referring to emotional distress[23] or depression.[24] Results for the SIPS are less conclusive as both a 3-factor model, with positive, negative, and general factors,[25,26] and a 4-factor model,[27] including positive symptoms, distress, negative symptoms, and deteriorated thinking, have been proposed.[28] For the SPI-A, a robust 6-dimensional model was reported in different samples from multidimensional scaling analyses[29] comprising emotional deficits, cognitive impediments, overstrain, cognitive disturbances, perception and motor disturbances, and body perception disturbances.

Despite the assumed dimensional overlap on a psychosis severity continuum, no study to date has investigated the symptom structure of these different measures. For this purpose, in our highly original study, we examined the commonalities of the symptom space as assessed with the SPI-A, SIPS, and PANSS using a very recent and innovative network approach.[30,31]

So far, orthogonal factor or principal component analyses have predominately been used in studying the symptom dimensions in PANSS and SIPS.[23–27] Both analyses assume different factors as independent of each other. In contrast, similar to the infrequently applied oblique factor analyses[28] that assume interrelation of latent variables, network approaches regard clinical symptoms not as distinct entities but as etiologically connected[30,32] (supplementary etext 2). Thus, revealing the full scale of interrelations using network analysis[30] might have clinical relevance, as "core" symptoms of subnetworks that are highly connected to other symptoms of their subnetwork are supposed to be the most crucial treatment targets in psychosis.[30,33–40] Knowing and targeting such "core" symptoms specifically in the early states might thus prevent progression to psychoses. Using the network approach has already deepened the understanding of the relation of schizotypy and schizotypal personality disorder dimensions,[41,42] such as by showing that social anhedonia seems to bridge the positive and negative schizotypy factor, thus clarifying earlier conflicting results on their relation.[41]

Because models of emerging psychosis[3,7,18] are still lacking empirical support, particularly with regard to the relationship of items of the SPI-A, SIPS, and PANSS, the main goal of our study was to estimate the network structure of the basic, attenuated, and frank psychotic symptoms and related symptoms in subjects attending an early recognition and intervention center. Thereby, we did focus on patients with CHR status or FEP and, for the importance and high prevalence of depression in early states of psychosis,[43] also on service users with depression (supplementary etext 3). Secondary goals were to identify central symptoms of possible subnetworks and symptoms bridging these possible subnetworks (shortly called as "bridge symptoms"). We hypothesized that, for their close conceptual relation, related symptoms of attenuated and frank psychotic symptom measures would strongly correlate in one main subnetwork with possible secondary subnetworks according to the commonly identified factors (positive, negative, and general), and that basic symptoms would also correlate according to the identified 6 dimensions in a second main subnetwork. Further, we expected that symptoms relevant to CHR criteria would be closely interrelated both within and across subnetworks.

Methods

Participants

Our analysis sample contained 460 patients of age 16–40 (table 1) who had sought help at the Cologne Early Recognition and Intervention Centre for mental crises (FETZ) and participated in either of 2 studies[44–47] (supplementary etext 4 and etable 3 detail the studies and sampling). Of these, 203 were considered at CHR (44.1%) by UHR or basic symptom criteria,[11,48] 153 had a first episode of schizophrenia (33.3%), and 104 suffered from a nonpsychotic, non-CHR depressive episode (22.6%). Exclusion criteria of both the studies were a somatic or drug-related condition explaining the mental condition and, in CHR and depression patients, lifetime diagnosis of psychosis and any missing data on any of the 3 target scales. All subjects had provided written informed consent. The local Ethical Committee of the Medical Faculty of the University of Cologne had approved the studies.

Assessments

Patients were assessed for basic symptom criteria with the SPI-A,[17] for UHR criteria with the SIPS, versions 2.1 and 3,[12–14] and for frank psychotic symptoms with the

Table 1. Sociodemographic and Clinical Characteristics of the Help-Seeking FETZ Sample (N = 460)

	Major Depression (n = 104)	Clinical High Risk (n = 203)	First-Episode Psychosis (n = 153)	Total Sample[f] (N = 460)	χ^2/U	df	P-Value
Age in years: mean (SD)	27.5 (7.4)	25.3 (5.6)	26.7 (6.5)	26.2 (6.4)	6.423	2	.040
Sex: % males	51.0	65.0	74.5	65.0	15.091	2	.001
Current partnership: % single	64.7	60.5	77.1	67.8	11.751	2	.003
Marital status: % never married	77.7	88.2	83.0	84.1	5.844	2	.059
Highest school graduation[a]: %					28.132	4	<.001
still in school[b]	7.9	15.2	3.3	9.7			
ISCED 2	31.7	24.8	47.0	33.7			
ISCED 3	60.4	59.9	49.7	56.6			
Current occupation: %					16.754	6	.010
regular occupation incl. school	72.5	78.5	59.5	70.8			
unemployed	21.6	19.0	32.7	24.2			
sheltered work place	2.9	1.0	3.9	2.4			
sporadic employment	2.9	1.5	3.9	2.6			
CHR type[c]: %					not applicable		
only basic symptom criteria		25.5					
only ultra-high risk criteria		4.9					
both types of CHR criteria		69.5					
Conversion to psychosis[d], %	6.7	43.6			7.674	1	.006
% with follow-up	14.4	65.5			71.904	1	<.001
Follow-up in months: mean (SD)	38.6 (17.9)	34.8 (23.7)			0.484	1	.487
SOFAS[e]: mean (SD)	57.6 (17.5)	52.5 (16.9)	49.8 (10.5)	49.1 (15.0)	5.040	2	.080

Note: Kruskal-Wallis H-tests and χ^2 tests were used to analyze group differences.
[a]ISCED: International Standard Classification of Education, 2011 revision (http://www.uis.unesco.org/Education/ Pages/international-standard-classification-of-education.aspx). Description of main categories: 2: lower secondary education; 3: upper secondary education.
[b]Mainly aiming for ISCED 3.
[c]Not including the genetic risk plus functional decline criterion.
[d]Numbers relate to those with a follow-up in the respective group.
[e]Social and Occupational Functioning Assessment Scale.
[f]Medication was not formally assessed in the first-episode psychosis and depressive sample; yet antipsychotic medication can be assumed for the vast majority of, if not all first-episode psychosis patients at the time of the interview. Of the CHR patients, 12% had been prescribed an antipsychotic (mainly low dose) and 13% an antidepressant by the time of the interview.

PANSS[15] (supplementary etext 5, table 2). The German version of the Structured Clinical Interview for DSM-IV (SCID-I)[49] was used to assess axis-I disorders, including FEP and depression. Professionals who had been previously trained in these scales performed all interviews.

Data Analysis

In our symptom-related network approach, individual items (ie, symptoms) constitute *nodes*, whose associations form *edges*. These items tend to be positively skewed and, therefore, there is likely to be deviations from multivariate normality. For estimating the edges, partial correlations are chosen over zero-order correlation, because zero-order correlations can be spurious.[39] Given the nonparametric nature of the data, we first performed a nonparanormal transformation following the method for estimating sparse undirected graphs of high dimensionality.[50] Specifically, we used the *R* package *huge* and the *skeptic* options as the transformation function. Thus, we applied a Gaussian transformation to the data to help relax the normality assumption.[50] Next, a network was constructed by means of the *R* package *qgraph*,[51] using an iterative algorithm,[52] which forces embedded network layouts after 500 iterations. We used a direct application of the Fruchterman-Reingold algorithm that might lead to spurious correlations because we were interested in all symptom connections and not in an artificially constrained ("stripped") model of selected connections (supplementary etext 6).

In order to assess the distribution and importance of symptoms as nodes within the network, quantitative node centrality measures were applied based on means of *strength*, *betweenness*, and *closeness*, which, focusing on different aspects of node relevance and interconnectivity, are complementary. Thereby, *strength* is equal to the sum of the edge weights connected to a particular node. *Closeness* is an index of centrality defined as the inverse of the average shortest path length from one node to all other nodes in the network.[53] *Betweenness* is the fraction of all possible shortest paths that pass through a particular node.[53]

Table 2. Group Comparison of SPI-A, SIPS, and PANSS Symptoms Between First-Episode Psychosis (FEP), Clinical High Risk (CHR), and Major Depression (MD)

SPI-A symptom		% Present (score ≥ 1)	χ^2 (df = 2)	*P* Value	Post hoc Test Results
A1	Impaired tolerance to unusual, unexpected or specific novel demands	73.9	43.924	< .001	FEP > CHR = MD
A2	Impaired tolerance to certain social everyday situations	74.5	61.369	< .001	FEP > CHR > MD
A3	Impaired tolerance to working under pressure of time or rapidly changing different demands	77.1	49.431	< .001	FEP > CHR > MD
A4	Changes in mood and emotional responsiveness	96.4	4.502	< .001	FEP > CHR = MD
A5	Decrease in positive emotional responsiveness toward others	85.1	6.852	< .001	FEP = CHR > MD
B1	**Inability to divide attention**[a]	41.8	48.562	< .001	FEP > CHR > MD
B2	Feeling overly distracted by stimuli	47.4	38.561	< .001	FEP = CHR > MD
B3	Difficulties concentrating	90.6	25.877	< .001	FEP > CHR > MD
B4	Difficulties to hold things in mind for less than half an hour	62.6	43.837	< .001	FEP = CHR > MD
B5	Slowed-down thinking	62.6	15.096	< .001	FEP = CHR > MD
B6	Lack of thought energy. Purposive thoughts	64.2	40.345	< .001	FEP > CHR > MD
C1	Increased indecisiveness with regard to insignificant choices between equal alternatives	61.5	21.128	< .001	FEP = CHR > MD
C2	**Thought interference (B)**	47.6	65.711	< .001	FEP > CHR > MD
C3	**Thought blockages**	55.9	69.661	< .001	FEP = CHR > MD
C4	**Disturbance of receptive speech**	54.4	82.030	< .001	FEP = CHR > MD
C5	**Disturbance of expressive speech**	55.2	45.540	< .001	FEP = CHR > MD
C6	Disturbance of immediate recall	53.8	59.286	< .001	FEP = CHR > MD
D1	Decreased capacity to discriminate between different kinds of emotions	35.0	21.937	< .001	FEP = CHR > MD
D2	Increased emotional reactivity in response to routine social interactions	82.8	19.381	< .001	FEP > CHR = MD
D3	**Thought pressure (B)**	51.7	98.630	< .001	FEP > CHR > MD
D4	**Unstable ideas of reference**	56.4	122.866	< .001	FEP > CHR > MD
D5	**Changed perception of the face or body of others**	13.1	19.244	< .001	FEP > CHR > MD
E1	Bodily sensations of numbness and stiffness	15.6	11.682	.003	FEP > CHR = MD
E2	Bodily sensations of pain in a distinct area	17.5	8.668	.013	FEP = CHR > MD
E3	Bodily sensations migrating through the body	5.3	6.061	.048	FEP = CHR > MD
E4	Bodily sensations of being electrified	8.2	3.508	.173	FEP = CHR = MD
E5	Bodily sensations of movement or pressure	1.1	16.971	< .001	FEP = CHR > MD
E6	Bodily sensations of body/body parts changing size	8.3	8.433	.015	FEP = CHR > MD
F1	Hypersensitivity to light / optic stimuli	29.8	10.791	.005	FEP = CHR > MD
F2	**Photopsia**	10.2	4.868	.088	FEP = CHR = MD
F3	**Micropsia. Macropsia**	4.1	3.885	.143	FEP = CHR = MD
F4	Hypersensitivity to sounds/noise (B)	50.7	41.968	< .001	FEP = CHR > MD
F5	**Changed intensity/quality of acoustic stimuli (B)**	33.5	56.320	< .001	FEP > CHR > MD
F6	Somatopsychic bodily depersonalization	8.1	30.187	< .001	FEP = CHR > MD
O1	**Thought perseveration**	45.6	59.855	< .001	FEP > CHR > MD
O4.10	**Partial seeing including tubular vision**	8.1	8.753	.013	FEP = CHR > MD
O11	Loss of automatic skills	17.4	9.079	.011	FEP = CHR > MD

SIPS symptom		% Present (score ≥ 1)	χ^2 (*df* = 2)	*P* Value	Post hoc Test Results
P1	Unusual thought content / delusional ideas (B)	64.1	327.979	< .001	FEP > CHR > MD
P2	Suspiciousness / persecutory ideas (B)	56.5	224.593	< .001	FEP > CHR > MD
P3	Grandiosity	16.7	48.092	< .001	FEP > CHR > MD
P4	Perceptual abnormalities / hallucinations (C)	51.5	169.359	< .001	FEP > CHR > MD
P5	Disorganized communication (C) (B)	44.6	176.170	< .001	FEP > CHR > MD
N1	Social anhedonia or withdrawal (B)	73.7	88.458	< .001	FEP > CHR > MD
N2	Avolition	76.1	31.594	< .001	FEP > CHR > MD
N3	Decreased expression of emotion	48.6	71.400	< .001	FEP > CHR > MD
N4	Decreased experience of emotions and self	49.6	41.103	< .001	FEP > CHR > MD
N5	Decreased ideational richness	39.8	74.304	< .001	FEP > CHR > MD
N6	Deterioration in role functioning (B)	65.6	144.901	< .001	FEP > CHR > MD
D1	Odd behavior or apperance (B)	25.1	82.437	< .001	FEP > CHR > MD
D2	Bizarre thinking	29.5	147.272	< .001	FEP > CHR > MD
D3	Trouble with focus and attention	54.3	59.859	< .001	FEP > CHR > MD

Table 2. Continued

SIPS symptom		% Present (score ≥ 1)	χ^2 ($df = 2$)	*P* Value	Post hoc Test Results
D4	Personal hygiene / social attentiveness	36.4	65.281	< .001	FEP > CHR = MD
G1	Sleep disturbance	67.8	57.949	< .001	FEP > CHR > MD
G2	Dysphoric mood	83.3	41.442	< .001	FEP > CHR > MD
G3	Motor disturbances	26.6	43.137	< .001	FEP > CHR > MD
G4	Impaired tolerance to normal stress	62.2	92.888	< .001	FEP > CHR > MD
PANSS symptom		**% Present (score ≥ 2)**	**χ^2 ($df = 2$)**	***P* Value**	**Post hoc Test Results**
P1	Delusions (C) (B)	54.1	323.187	< .001	FEP > CHR > MD
P2	Conceptual disorganization (B)	42.5	158.552	< .001	FEP > CHR > MD
P3	Hallucinatory behavior (C)	42.3	178.026	< .001	FEP > CHR > MD
P4	Excitement (B)	49.6	115.759	< .001	FEP > CHR > MD
P5	Grandiosity	14.1	60.153	< .001	FEP > CHR > MD
P6	Suspiciousness (B)	52.0	215.481	< .001	FEP > CHR > MD
P7	Hostility (B)	22.4	74.665	< .001	FEP > CHR > MD
N1	Blunted affect (B)	46.4	128.659	< .001	FEP > CHR > MD
N2	Emotional withdrawal (B)	49.4	99.024	< .001	FEP > CHR > MD
N3	Poor rapport (B)	46.1	118.884	< .001	FEP > CHR > MD
N4	Passive-apathetic social withdrawal	68.9	99.547	< .001	FEP > CHR > MD
N5	Difficulty in abstract thinking (B)	33.5	115.227	< .001	FEP > CHR > MD
N6	Lack of spontaneity & flow of conversation	40.0	46.614	< .001	FEP > CHR > MD
N7	Stereotyped thinking (B)	41.6	137.145	< .001	FEP > CHR > MD
G1	Somatic concern	45.0	17.682	< .001	FEP > CHR > MD
G2	Anxiety	59.8	69.127	< .001	FEP > CHR > MD
G3	Guilt feelings	37.8	2.800	.247	FEP > CHR = MD
G4	Tension	79.1	71.219	< .001	FEP > CHR > MD
G5	Manierisms & posturing	15.8	59.638	< .001	FEP > CHR > MD
G6	Depression (B)	80.8	2.082	.353	FEP > CHR = MD
G7	Motor retardation	42.7	28.285	< .001	FEP > CHR = MD
G8	Uncooperativeness	19.6	46.924	< .001	FEP > CHR = MD
G9	Unusual thought content	33.7	144.471	< .001	FEP > CHR > MD
G10	Disorientation	7.4	33.679	< .001	FEP > CHR = MD
G11	Poor attention	44.5	80.760	< .001	FEP > CHR > MD
G12	Lack of judgement & insight	27.7	91.450	< .001	FEP > CHR > MD
G13	Disturbance of volition	28.8	34.491	< .001	FEP > CHR > MD
G14	Poor impulse control	37.5	23.121	< .001	FEP > CHR = MD
G15	Preoccupation	45.7	53.959	< .001	FEP > CHR > MD
G16	Active social avoidance	53.9	85.310	< .001	FEP > CHR > MD

Note: Kruskal-Wallis *H*-test and post hoc Mann-Whitney *U*-test (2-tailed *alpha* > 0.05) were used.
[a]**Bold** indicates SPI-A symptoms that are part of the basic symptom criteria, and SIPS and PANSS symptoms included in ultra-high-risk criteria. (B): bridge symptom. (C): central symptom.

Additionally, the robustness of the network was examined by stability analyses, investigating how likely a similar network, ie, comparable correlations between symptoms, would be found when constructing the same network in another sample[54] using a bootstrapping methodology.[55] For the sake of robustness, this procedure was repeated 1000 times using the *R* package *bootnet*. Additionally, 95% confidence intervals for edge weights from the bootstrapped sample were reported. Secondly, we also checked for the stability of node *strength*. We selected strength because it has been shown relevant for replication and network interpretation, ranking the node centrality that can be seen as a bridge between pathologies.[56] Specifically, statistically significant differences were verified based on a null-hypothesis test. A nonsignificant value means low variability (high stability) in the interrelationships between specific nodes.

Results

Symptom Frequency

Most SPI-A, SIPS, and PANSS symptoms were significantly more frequent in the psychosis than in the CHR group, and in both groups significantly more frequent than in the depression group (table 2).

Symptom Network Structure

Network analysis revealed one single network with 86 well-connected nodes without any subnetworks (figure 1), constituting a total of 3655 edges (or paths), of which

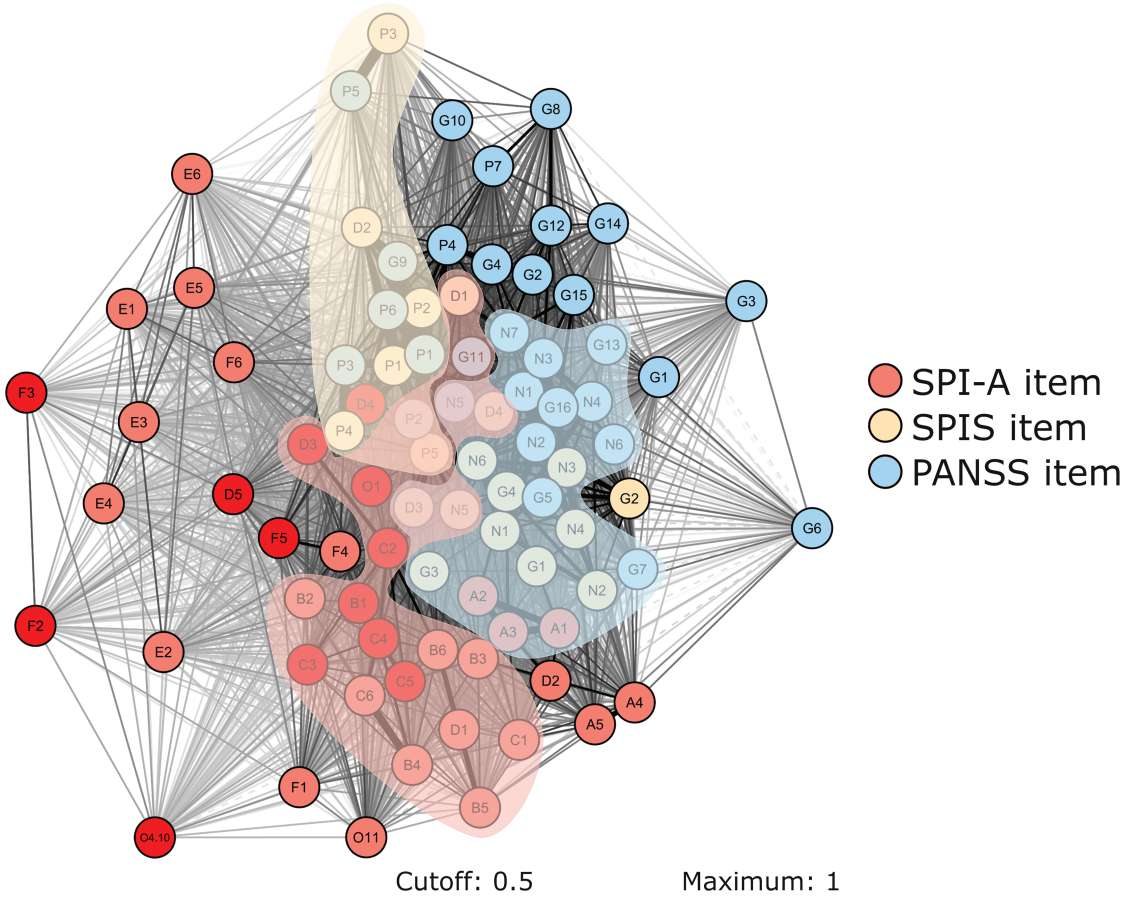

Fig. 1. Network structure of SPI-A, SIPS, and PANSS symptoms (N = 460). Numbers in nodes (symptoms) indicate their item number in the respective scale: SPI-A (red nodes, with dark-red indicating criteria-relevant basic symptoms), SIPS (yellow nodes), and PANSS (blue nodes). The lines' type represents the direction of correlation between 2 nodes with continuous line indicating positive and dotted lines indicating negative correlations. The lines' thickness represents the correlation between the 2 connected nodes with thicker line indicating higher correlation. The lines' length, ie, the distance between 2 nodes, corresponds to the absolute edge weight between these nodes, with edge weights representing the similarity between nodes so that similar nodes are close to each other and dissimilar nodes far from each other. Nodes within the red border may be considered as part of the cognitive-disorganized subgroup, those within the yellow border as part of the positive subgroup, and those within the blue border as part of the negative subgroup. All nodes not within a border to the right may be considered as part of the affective subgroup, those not within a border to the left as part of the (body) perception subgroup (see also main text).

3600 (98.5%) indicated positive associations. Most relevant symptoms—either central symptoms (C) or symptoms bridging different dimensions (B)—are indicated by the respective letter in table 2.

Symptoms of the 3 scales showed a progressive diagonal pattern, mainly with SPI-A symptoms from the left lower part of the network via mid-positioned SIPS to PANSS symptoms in the upper right part. The main amalgamation of scales was between the corresponding and strongly connected positive symptoms of SIPS and PANSS. While most symptoms closely centered together, the few peripheral SPI-A and PANSS symptoms included visual (SPI-A-F2-3, -O4.10) and body perception disturbances (SPI-A-E1-4, -E6), and also depression (PANSS-G6) and guilt feelings (PANSS-G3) (figure 2b).

The outstanding most central symptom was the SIPS disorganized communication (SIPS-P5) but not the corresponding, closely associated PANSS-P2 conceptual disorganization (Figure 2a–c; supplementary etext 7 and efigure 1 provide expected influence values). Yet, also the 2 highly interconnected hallucinatory items of SIPS (P4) and PANNS (P3) and PANSS delusions (P1) were closely and, at least at trend level, statistically significant connected by short paths to other nodes (figure 2c); SIPS items P1, P2, and P3 that were closely linked to PANSS-P1, however, demonstrated no such high betweenness. SPI-A symptoms were mostly linked to the center of the network (ie, SIPS-P5) via thought interference (SPI-A-C2), which was also closely connected with other cognitive basic symptoms included in CHR criteria (figure 1).

Stability of the Network

Confidence intervals of most edges did not contain zero (figure 3a), meaning that most relationships between symptoms are higher than chance level. Additionally, some

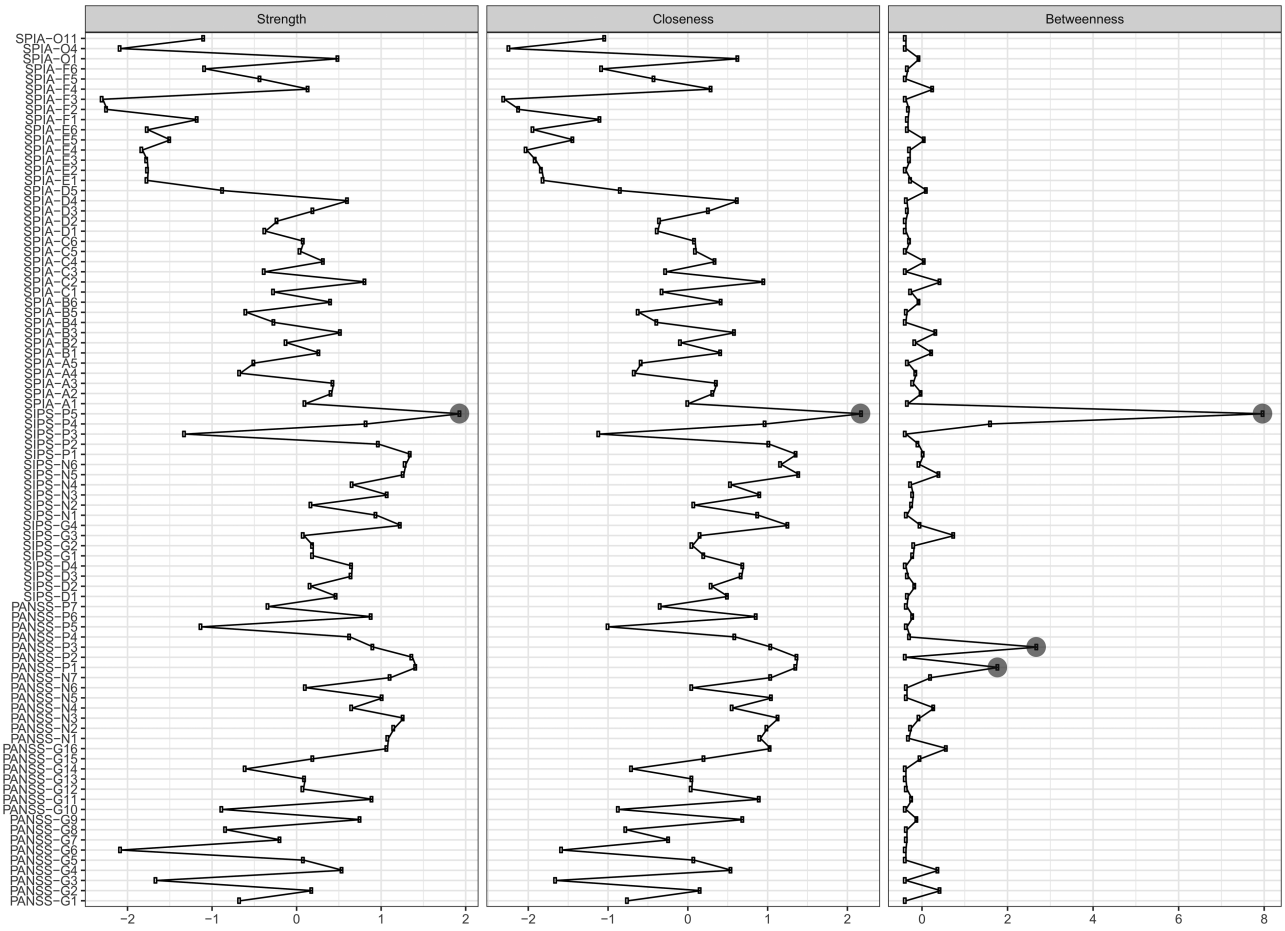

Fig. 2. Centrality measures of nodes (symptoms) within the network. Gray areas indicate at least statistical trend level (*alpha* ≤ 0.10) for low (left) or high (right) centrality measures of single nodes ($z \geq |1.645|$). Strength indicates the strength of the direct association of one node with others. Closeness gives a measure of the average length of shortest paths between one node and all others; high values indicate that the node is close to others, whereas low numbers indicate that it is rather distant from others. Betweenness indicates the number of shortest indirect paths between nodes crossing through the node, thus representing its importance as a kind of "relay station."

confidence intervals had overlapping edges, indicating a possible lack of significant differences between them. Moreover, most nodes revealed statistical differences between them in terms of node strength (figure 3b). Taken together, these results indicate not only a high robustness and stability of the obtained network but also a possibly limited generalizability to other populations.

Discussion

For the first time, we analyzed the common structure of various symptoms associated with and relevant for (early) psychosis, ie, not only frank symptoms of the PANSS but also attenuated and basic symptoms and related symptoms using SIPS and SPI-A, using a network approach. To the best of our knowledge, network analysis of relevant symptoms for psychosis has so far been performed mainly in patients suffering from schizophrenia or other non-affective psychoses using the PANSS or similar scales, usually restricted to sum scores.[35,57] Our study is also the first to include not only CHR patients but also depressive patients, the latter because of the close link between depression and psychosis, especially in the early states[43,45,58,59] (supplementary etext 3). Bringing these 3 diagnostic groups together allows conclusions not only about the diagnostic specificity of symptoms when comparing FEP to depression, but also about the course of the disease when comparing CHR with FEP.

Central Symptoms and Symptom Subgroups

Contrary to the two expected main subnetworks, our analyses revealed a single network reflecting symptom severity and related assessments from subjective basic symptoms via more observable attenuated to manifest symptoms. Therein, the symptoms, which are relevant for diagnosis of schizophrenia and employed in the definition of the symptomatic UHR-criteria according to the different scales,[16] ie, delusions (PANSS-P1), hallucinations (SIPS-P4, PANSS-P3), and—above all—disorganized communication (SIPS-P5), were strongly interrelated core symptoms. Despite the network's density, based on the position and

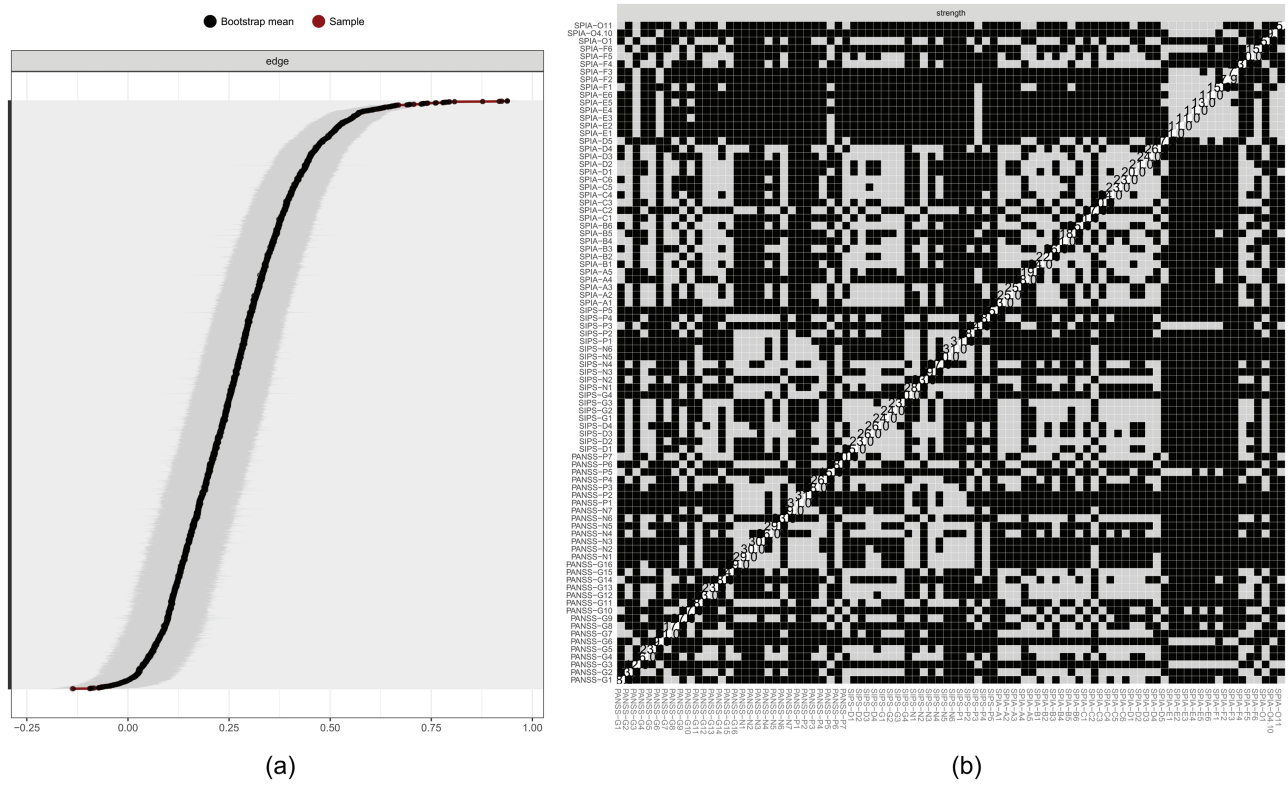

Fig. 3. Edge and node strength stability. (a) Bootstrapped confidence interval (95%, gray area) of all the edge weights. Every horizontal line represents a certain edge weights between 2 symptoms (3655 edges). For the sake of clarity, the labels are deleted. A top-down ordering is applied, so that the highest edge weight is at the top (of the Y-axis) and the lowest edge weights are at the bottom. When confident intervals (in gray) show considerable overlap, the edge weights might not significantly differ from each other. Likewise, when the gray area contains zero, the correlation is not statistically significant (ie, does not differ from random association). (b) Bootstrapped stability test for node strength. Each matrix element corresponds with a direct comparison between 2 nodes (*alpha* = 0.05). Statistically significant differences are indicated by a black box, and nonsignificant ones by a gray.

nature of symptoms and roughly corresponding to the 5-factor structure described for the PANSS,[23,24] 5 partly overlapping symptom subgroups were discernible with positive, negative, and cognitive-disorganized symptoms forming the core, and (body) perception and affective symptoms building the periphery. Within these subgroups, the symptoms relevant for CHR criteria were mainly part of the positive and cognitive-disorganized subgroup, whereby, supporting our expectations, attenuated positive and, especially cognitive, basic symptoms were in close distance.

For the clinic, central[31,34–40] and bridge symptoms, ie, symptoms that are connected with symptoms of both their own and other subgroups and, thus, *bridge* different subgroups, might be especially important treatment targets, as they might exacerbate symptoms of the linked subgroup.[31,32] Such bridge symptoms can be identified by inspecting their single correlations, and also their strength and closeness measures.

With regard to the central positive subgroup, the slightly more peripheral position of the rarely occurring grandiosity (SIPS-P3, PANSS-P5) was striking and, for their close relation to the affective symptom mania, might have indicated their assignment to the affective subgroup. Yet, inspection of descriptive measures indicated a closer link with the positive than the affective subgroup, which is in line with earlier findings on SIPS and PANSS.[23–26,28,39] Similarly, conceptual disorganization (SIPS-P5, PANSS-P2) might be placed in both the positive and the cognitive-disorganized subgroup, to which they were equally linked according to their descriptive measures. In factor analyses of SIPS or PANSS, conceptual disorganization commonly joined the disorganization and not the positive factor,[23–28] although, in a recent network analysis of the PANSS, conceptual disorganization was part of the positive dimension.[40] Future analyses, such as modularity measures,[60] might clarify the status of conceptual disorganization in complex networks.

Other overlaps occurred between negative and cognitive-disorganized subgroups for symptoms capturing difficulties in concentration/attention problems (SPIS-D3) and abstract thinking (SIPS-N5, PANSS-N5), and also problems in personal hygiene (SIPS-D4). Again, inspection of the correlation matrix indicated their better placement in the cognitive-disorganization subgroup. The non-placement in the negative subgroup was mainly in line with earlier findings that did not place the 3 cognitive items in pure negative dimensions.[23–28,39] Yet, contrary to our placement, problems in personal hygiene (SIPS-D4) was mainly placed with the negative symptoms in earlier factor analyses.[25,26,28]

Bridge Symptoms

Difficulty in abstract thinking (PANSS-N5) of the cognitive-disorganized subgroup and of the negative subgroup, stereotyped thinking (PANSS-N7), poor rapport (PANSS-N3), blunted affect (PANSS-N1), emotional withdrawal (PANSS-N2), social anhedonia (SIPS-N1), and deterioration in role functioning (SIPS-N6) were significantly correlated to a variety of positive features. In an earlier less dense network of only positive and negative PANSS items and a depression scale,[39] difficulty in abstract thinking (PANSS-N5) and stereotyped thinking (PANSS-N7) were part of the positive cluster and mainly linked the negative and positive cluster, predominately via poor rapport (PANSS-N3), lack of spontaneity (PANSS-N6), and passive social withdrawal (PANSS-N4) of the negative cluster.

The affective peripheral PANSS items such as depression (G6) and guilt feelings (G3) were unrelated to the positive subgroup; rather, depression was mainly, though still weakly, linked to the negative dimension by avolition (SIPS-N2) and passive social withdrawal (PANSS-N4). In the earlier network,[39] the depression cluster, which solely comprised items of the depression scale, was only weakly linked to the negative cluster, whereas the positive cluster was mainly linked by suspiciousness (PANSS-P6) and guilt ideas of reference. In our network, the affective subgroup was linked to the positive subgroup mainly by excitement (PANSS-P4), indicating that high excitement (PANSS-P4)—if not treated early—might trigger exacerbation of positive symptoms. This corresponds well with current models of the role of stress in developing or maintaining positive symptoms of psychosis.[61–63]

Of the positive subgroup, suspiciousness/paranoid ideas (PANSS-P6, SIPS-P2) mainly linked to the affective subgroup, especially via excitement (PANSS-P4) and hostility (PANSS-P7), a link well established in the clinical literature.[64–67] Further, the positive subgroup was linked to the negative subgroup mainly via the core item disorganized communication (SIPS-P5) and its counterpart (PANSS-P2), and, additionally, by unusual thought content/delusions (SIPS-P1, PANSS-P1). The same showed the connection between the positive and cognitive-disorganized subgroups. This indicates that the large variety of non-paranoid, non-grandiose (attenuated) delusional ideas, including "Ich-Störungen," might be particularly prone to be followed or accompanied by negative and cognitive-disorganized symptoms. Indeed, literature on delusional disorders, which are by definition not accompanied by significant negative and cognitive-disorganized symptoms, indicates a dominance of paranoid and grandiose ideas.[68,69]

The cognitive-disorganized and the positive subgroup were linked, besides the strong role of disorganized communication (SIPS-P5, PANSS-P2) again, mainly by odd behavior/appearance (SIPS-D1), observed difficulty in abstract thinking (PANSS-N5), subjective thought pressure (SPI-A-D3), and subjective thought interference (SPI-A-C2). The role of cognitive disturbances in the development of positive symptoms is well established by literature on the early detection of psychosis.[19,20,70,71] Furthermore, together with the central role of disorganized communication (SIPS-P5, PANSS-P2), this finding corroborates conceptualizations proposing that psychiatric disorders are essentially communication disorders,[72,73] thus emphasizing the role of objective and subjective symptoms in thought and language[74] that should be addressed early by language and communication approaches.[75]

The role of odd behavior/appearance (SIPS-D1) is less clear. Although disorganized symptoms, apart from disorganized communication, were reported to contribute to psychosis development,[76,77] odd behavior/appearance was commonly not particularly predictive and, thus, might play a more important role in transmitting heightened disorganization levels extended by other, more predictive disorganization symptoms.

Regarding the peripheral (body) perception disturbances, hypersensitivity to sounds/noise (SPI-A-F4) was mostly linked to symptoms of the positive and cognitive-disorganized subgroup. In addition, the changed intensity/quality of acoustic stimuli (SPI-A-F5) was linked to positive symptoms. This might reflect the dominance of auditory hallucinations compared to visual ones in adult psychosis patients, either alone or in association.[78,79] Furthermore, in patients with auditory hallucinations with a negative affect (anxiety, depression, or stress), beliefs of uncontrollability or worry might potentially result in paranoia.[80]

Thus, regarding the bridge symptoms, several criteria- and/or diagnostically relevant symptoms were found among them, supporting their role in the possible exacerbation of the disorder.[7–10] Of the basic symptoms, these were thought pressure (SPI-A-D3), thought interference (SPI-A-C2), and changed intensity/quality of acoustic stimuli (SPI-A-F5). With regard to the UHR criteria, these were non-grandiose delusions (PANSS-P1, -P6, SIPS-P1, -P2), hallucinations (PANSS-P3, SIPS-P4), and disorganized communication (PANSS-P2, SIPS-P5).

Strengths and Limitations

Our study has several strengths and limitations (supplementary etext 8 provides details). In brief, among the strengths is the use of network analysis, a promising new approach that can be seen in the long tradition of the "concept of emergence"[81,82] and gives significant insights into psychopathological pathways and, thereby, may be used as a starting point for personalized medicine.[31] Yet, results of network analyses might be group- and/or state-dependent.[83–85] However, our diagnostically diverse sample of early detection service users may be more generalizable.

The high amount of missing data for 8 criteria-relevant SPI-A symptoms and the noninclusion of potentially relevant objective neurocognitive, quality of life, and functional measures might be seen as limitations.

Conclusions

Our sample of patients clinically suspected to develop psychosis and, thus, referred to an early detection service revealed a dense network of highly interrelated symptoms across the 3 different assessment scales that, yet, was distinguished by symptom severity. Furthermore, it revealed a central role of positive symptoms (except grandiosity) that, from the perspective of more subtle subjective symptoms, seem to develop from cognitive and perceptual disturbances included in basic symptom criteria. If supported in future prospective studies, these central symptoms and the symptoms "bridging" the association between the 5 symptom subgroups may be regarded as target symptoms to prevent symptomatology from spreading or increasing across the whole network.

Supplementary Material

Supplementary data are available at *Schizophrenia Bulletin* online.

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