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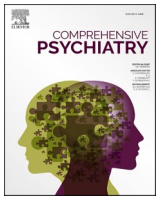

Impact of psychopathology on day-to-day living in patients with schizophrenia: A network analysis

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ABSTRACT

Although the relationship between schizophrenia and disability is well established, the association between the symptoms of the disorder and functional domains remains unclear. The current study explored the nuances of the relationship between symptoms and domains of functioning in a sample of 1127 patients with schizophrenia. We assessed the symptoms of schizophrenia with the Positive and Negative Syndrome Scale (PANSS) and psychosocial functioning with the mini-ICF-APP (mini-International Classification of Functioning Rating for Limitations of Activities and Participation in Psychological Disorders). The mean PANSS score was 94.28 (27.20), and the mean mini-ICF-APP score was 25.25 (8.96), both of which are indicative of severe symptom load and impairment. We were able to show a strong relationship and overlap between symptoms and disability in patients with schizophrenia. We identified several symptoms related to functional impairment. Deficits in judgment and abstract thinking contribute to impairment through poor adherence (to routines and compliance with rules) and difficulties in planning and organizing. We believe that in schizophrenia, symptoms and their interactions constitute a disorder beyond any single manifestation. Furthermore, we suggest that cognitive testing and cognitive treatment should become part of the standard of care for patients with schizophrenia.

1. Introduction

Schizophrenia is a severe, often enduring, and sometimes treatment-resistant mental disorder [32,37]. Despite the manifest clinical presentation of schizophrenia, its neurobiological underpinnings have yet to be clarified. There may be high genetic heterogeneity within the broad diagnosis of schizophrenia, as well as generally high interindividual variability in neurobiological markers of schizophrenia [28,29,32]. Therefore, characterizing schizophrenia based on psychopathology and behavioral markers using well-established, easy-to-implement measures and assessment methods still yields highly relevant insights into the nature of the disorder [29,32].

The phenomenology of schizophrenia is complex and traditionally subdivided into three main domains: positive symptoms (i.e., hallucinations, delusions, and thought disorders), negative symptoms (i.e., scarcity of thought, and lack of affect) and cognitive symptoms (i.e., working memory, and executive functions) [32]. In addition, patients with schizophrenia experience nonspecific symptoms or general psychopathology (e.g., anxiety, feelings of guilt, tension, depression) [24,32]. In addition to its phenomenological and psychopathological characteristics, schizophrenia is also associated with a substantial long-term burden and low psychosocial functioning; affected people frequently struggle with the challenges of daily life [24,32,47]. The nature of the relationship between symptoms and psychosocial functioning is important since psychosocial functioning is linked to impairment and low quality of life [12,14,39]. Furthermore, the relationship between psychopathology and psychosocial functioning in schizophrenia patients suggests that the impairment of psychosocial functioning can be a manifestation of the disorder itself [18].

Thus, one line of interest and research is the relationship between the symptom domains of schizophrenia and psychosocial functioning or impairment [4]. Network analytic methods are uniquely suited for such investigations. The network approach conceptualizes mental disorders as complex, dynamic systems in which the causal interaction of

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symptoms constitutes the disorder [2]. In this study, we were not only interested in the relationships between symptoms of schizophrenia but also aimed to identify which symptoms connected the symptom domains and psychosocial functioning (using bridge centrality). Identifying these bridge symptoms that connect the two constructs might help to identify treatment targets.

2. Methods

2.1. Study design and sample population

The Department of Adult Psychiatry and Psychotherapy, as part of the Psychiatric University Hospital of Zurich, is responsible for the treatment of adult patients (aged 18 to 65) in the city of Zurich, Switzerland, and its surroundings, with a catchment area of approximately 500,000 inhabitants. The Center for Integrative Psychiatry specializes in the treatment of patients with severe and recurrent psychiatric disorders, such as psychotic disorders. A series of psychometric measures were used to assess disease severity and psychosocial functioning for each patient. Between January 1st, 2013, and December 31st, 2020, we systematically collected the psychopathological status and level of psychosocial functioning of patients with schizophrenia hospitalized for treatment. The Canton of the Zurich Ethics Committee authorized the use of anonymized data for research and publication purposes (BASEC: 2018-01906). The reporting of our study and results followed the STROBE guidelines and the recommendations for network analysis [5,49].

2.2. Clinical assessment and diagnosis

Attending psychiatrists, psychiatric residents, or clinical psychologists completed the clinical rating through a semistructured interview and clinical observation. The raters had a standardized introduction to the rating instruments. Psychiatric diagnoses were made by the clinician responsible for the treatment according to the International Classification of Disease 10 (Diagnostic Criteria for Schizophrenia [ICD-10] Chapter F20) [40] and validated by a board-certified senior psychiatrist.

2.3. Clinical rating scales

2.3.1. The positive and negative syndrome scale (PANSS)

The Positive and Negative Syndrome Scale (PANSS) was developed to measure changes in a comprehensive set of psychopathologic symptoms present in patients with schizophrenia. It consists of 30 single items (for a list of the single items, see Figs. 2 and 3). The PANSS was administered in semistructured interviews; each item was evaluated according to a seven-item Likert scale ranging from "1" (not present) to "7" (extremely severe), with a manual defining each item and the boundaries for categorization. Thus, the PANSS ranges between 30 and 210, with higher scores indicating more severe symptomatology [22]. The PANSS was initially categorized into three domains: positive, negative, and general symptomatology. However, five dimensions (positive, negative, cognitive, affective, and resistance) have been proposed and repeatedly validated [44].

2.3.2. mini-ICF-APP

The mini-ICF-APP (mini-International Classification of Functioning-Rating for Limitations of Activities and Participation in Psychological Disorders) was developed as a short observer-rated scale to assess the level of psychosocial functioning in individuals with mental health disorders as defined by the WHO International Classification of Functioning [27]. It consists of thirteen item domains (for a list of the single items, see Figs. 2 and 3.). Each item is rated on a five-point Likert scale from "0" (no disability) to "4" (total disability). The manual provides definitions for each item. Capabilities must be assessed in a specific context (e.g., workplace, work in general, household). The scale ranges from 0 to 52 points, with higher scores indicating more significant disability [27].

2.3.3. Clinical global impression, severity scale (CGI-S)

The CGI-Severity Scale consists of one question: *"Considering your total clinical experience with this particular population, how mentally ill is the patient at this time?"*, which is coded on a seven-point Likert-like scale ranging from "1" (normal) to "7" (among the most extremely ill patients), with "2" (borderline mentally) defining the transition to a psychiatric disorder [16].

2.4. Statistical analysis

We used simple descriptive statistics (proportion, mean, and standard deviation) to present the demographic and clinical characteristics of the sample. We used Cronbach's alpha coefficient to evaluate the reliability of the PANSS and the mini-ICF-APP. We analyzed the relationship between symptoms and psychosocial functioning using three complementary methods. First, we calculated the correlation between the PANSS score and the mini-ICF-APP sum score using Pearson's correlation. Second, we calculated the concordance correlation coefficient using the z scores to examine the level of accuracy and precision between the two measures [23,26]. Third, we used the Bland–Altman plot to infer the agreement between the PANSS and the mini-ICF-APP scale scores. For each participant, the difference between the two scales was plotted on the y-axis, the mean was plotted on the x-axis, and the confidence intervals and limits of agreement were calculated [6,30]. Finally, we calculated the correlation between the different dimensions of the PANNS (both three- and five-factor models) and the mini-ICF-APP; afterward, we performed pairwise calculations if the correlation differed from the global PANSS score [8].

We conducted a network analysis to explore the nuances of the relationships between psychopathological symptoms and domains of psychosocial functioning. In network models, variables are presented as nodes connected via edges, representing undirected regularized partial correlations [2]. Next, we estimated the network using a regularization technique based on the least absolute shrinkage and selection operator (LASSO) and the extended Bayesian information criterion (EBIC) for model selection. Through the LASSO-EBIC approach, low-threshold associations were reduced to zero, which reduced the false positive rate. Thus, the network presented is restricted to salient associations in the network. [10,11]. Network stability and reliability analyses were carried out using the bootnet package [10].

To describe the network's topological properties, we used network centrality measures (strength, closeness, betweenness, expected influence, and bridge influence). The node strength sums the absolute edge weights of the edges per node. Node closeness quantifies the distance between the node and all other nodes by averaging the shortest path lengths. The node betweenness metric quantifies how often a node lies on the shortest path connecting two other nodes. The node expected influence considers the sign of the edge weight; this approach is suited for nonarbitrary coding of variables (i.e., when higher values indicate more psychopathology or impairment); it quantifies how much variance is explained by its neighbors. The expected influence of a node bridge quantifies the variance of a node that is explained by another construct or dimension, in our case, how psychopathology spreads to psychosocial impairment. To identify the most influential nodes (i.e., items), we normalized the centrality indices and identified those indices above the 95th percentile [2,20,33].

For the statistical analyses and figures, we used RStudio (2024.04.1 + 748); the statistical software R (4.4.0); the R packages *tidyverse* (2.0.0); *cocor* (1.1–4); *ltm* (1.2–0); *blandr* (0.5.1); *qgraph* (1.9.8); *bootnet* (1.6); and *networktools* (1.5.2).

3. Results

3.1. Demographic and clinical characteristics of the sample

A total of 1127 patients with schizophrenia were included in the analysis. The mean age of the participants was 38.03 (11.17) years, and just over half of the participants were males (51.9%, $n = 589$). The vast majority were single (72.0%; $n = 812$), almost half had just completed regular (mandatory) education (50.4%: $n = 569$), one-third (33.5%; $n = 377$) had completed apprenticeship, and one-third (16.1%: $n = 181$) had completed college or university education. On average, the patients received two treatments as inpatients, with a mean length of stay of 53.52 (46.92) days for the current hospitalization. The patients had a mean CGI-S score of 5.88 (0.85). The patients had a mean PANSS score of 94.28 (27.20) points, with a mean score on the positive symptom subscale of 21.72 (8.45) points on the negative subscale of 25.33 ± 8.45 points and on the general subscale of 47.22 (13.89) points. The mean mini-ICF-APP score was 25.25 (8.96). For further details, see Table 1.

3.2. Psychometric properties of the symptom (PANSS) and functional (mini-ICF-APP) scales

We analyzed the psychometric properties of both scales and the overlap between both constructs. Our sample's PANSS and mini-ICF-APP scores had an excellent internal consistency, with Cronbach's alpha values of 0.92 and 0.91, respectively. The Pearson correlation coefficient between the two scales was 0.68 (95% CI: 0.65 to 0.71); for further details, see Fig. 1A. The concordance correlation coefficient was 0.63 (95% CI: 0.60 to 0.67). The Bland–Altman plot showed good agreement between the PANSS score and mini-ICF-APP score, with an upper limit of agreement of 1.66 (95% CI = 1.55 to 1.76) and a lower limit of agreement of −1.66 (95% CI = -1.76 to −1.55). Seventeen (0.02) values were outside the boundaries; for further details, see Fig. 1B.

Table 1
Demographic, clinical, and psychometric characteristics of the sample ($n = 1127$).

Demographic characteristics	*M (S.D.)*
Age (years)	38.03 (11.17)
	n (%)
Sex	
Female	542 (48.1)
Male	585 (51.9)
Civil Status	
Married	62 (5.5)
Separated/Divorced	245 (21.7)
Single	812 (72.0)
Widowed	8 (0.7)
Residence Status	
Migrant	160 (14.2)
Swiss	921 (81.7)
Refugee/Other	46 (4.1)
Education	
Regular School	569 (50.4)
Apprenticeship	377 (33.5)
College/University	181 (16.1)
Clinical Characteristics	*M (S.D.)*
Previous Hospitalizations	2.14 (1.19)
Duration of Treatment (days)	53.52 (46.92)
Psychometric Characteristics	
CGI-S	5.88 (0.85)
PANSS Global Scale	94.28 (27.20)
PANSS (Three Factor Model)	
Positive Dimension	21.72 (8.45)
Negative Dimension	25.33 (8.45)
General Dimension	47.22 (13.89)
PANSS (Five Factor Model)	
Positive Dimension	15.44 (6.95)
Negative Dimension	23.36 (8.43)
Cognitive Dimension	27.14 (9.72)
Affective Dimension	15.46 (5.52)
Resistance Dimension	10.17 (5.21)
mini-ICF-APP	25.25 (8.96)

The Pearson correlation coefficients between the mini-ICF-APP score and each of the three dimensions of the PANNS were 0.55 (95% CI = 0.51 to 0.59) for the positive dimension, 0.59 (95% CI = 0.55 to 0.63) for the negative dimension, and 0.63 (95% CI = 0.59 to 0.57) for the general psychopathological dimension; all correlations were lower ($p < .001$) than those for the global PANSS score. For the five dimensions of the PANSS, the Pearson correlation coefficients with the mini-ICF-APP were as follows: 0.50 (95% CI = 0.45 to 0.54) for the positive dimension, 0.52 (95% CI = 0.48 to 0.56) for the negative dimension, 0.64 (95% CI = 0.61 to 0.68) for the cognitive dimension, 0.38 (95% CI = 0.33 to 0.43) for the affective dimension, and 0.48 (95% CI = 0.44 to 0.53) for the resistance dimension; all correlations were lower ($p < .001$) than those for the global PANSS score. Thus, none of the dimensions (neither the three-factor nor the five-factor model) of the PANSS had a higher correlation with the mini-ICF-APP score than the PANSS global score.

3.3. Network analysis of symptoms and functional domains

We constructed a network model of symptoms and functional domains to examine the similarities and differences between the two constructs (i.e., symptoms and psychosocial functioning). The network included 43 nodes (items), and in the symptom network, the nodes had an average strength of 0.59 (0.20). Nodes N01 (blunted affect), G02 (anxiety), G04 (tension), and G07 (motor retardation) had the greatest strength. In the functionality network, the nodes had a mean strength of 0.73 (0.15); node F02 (planning) had the greatest strength (for further details, see Fig. 2).

In the symptom network, nodes had a mean closeness of 0.85 (0.08), and in the function network, nodes had a mean closeness of 0.88 (0.07). The symptoms associated with greater closeness in the symptom network were G07 (motor retardation) and G08 (uncooperativeness). In the functionality network, the mean closeness was 0.88 (0.07); node F02 (planning) had the greatest degree of closeness (for further details, see Fig. 2).

In the symptom network, nodes had a mean betweenness of 0.37 (0.27), with nodes N01 (Blunted Affect) and G02 (Anxiety) showing higher betweenness grades. The nodes in the functionality network had a mean betweenness of 0.54 (0.34), with node F02 (Planning) having the highest betweenness (for further details, see Fig. 2).

In the symptom network, the mean expected influence was 0.57 (0.26), with nodes N05 (Abstract Thinking), N06 (Lack of Spontaneity), G08 (Uncooperativeness), and G06 (Depression) showing a greater influence on the network. The functionality network had a mean expected influence of 0.64 (0.24), with node F02 (Planning) having the highest expected influence (for further details, see Fig. 2).

In the symptom network, the mean bridge influence had a mean of 0.11 (0.09); the nodes with the highest bridge influence were G12 (lack of judgment) and N05 (abstract thinking). In the functionality network, the nodes had a mean bridge influence of 0.24 (0.19), with node F01 (Adherence) showing the greatest bridge influence (for further details, see Fig. 2).

Fig. 3 displays the final network model. The network stability index was 0.75 (i.e., the maximum proportion of cases that could be dropped and still retained a correlation over 0.70 with the original estimate in 95% of the samples).

4. Discussion

Our study aimed to investigate the relationship between

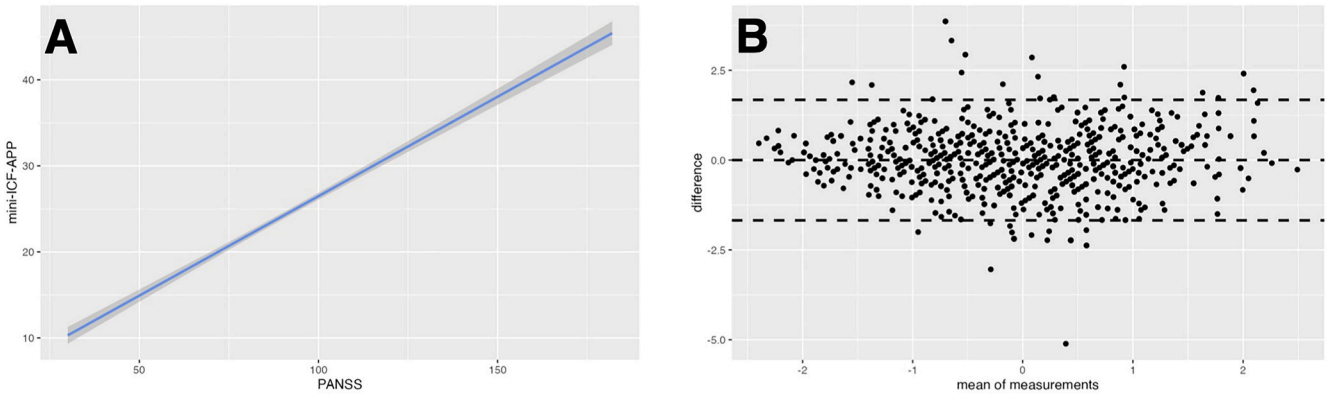

Fig. 1. A and B show the correlation overlap and agreement between the PANSS and mini-ICF-APP scales.
A Correlation between the PANSS score and mini-ICF-APP scale score. B: Bland–Altman plot between the PANSS score and mini-ICF-APP score. For each participant, the difference between the PANSS and mini-ICF-APP scores was plotted on the y-axis, while the mean of the PANSS and mini-ICF-APP scores was plotted on the x-axis.

psychopathological symptoms (as assessed by the PANSS) and functional impairment (as assessed by the mini-ICF-APP) in patients hospitalized for the treatment of schizophrenia. We employed a network analytic approach to calculate and visualize the complex interplay between symptoms, behavior, and functional domains, especially focusing on symptoms connecting these domains using bridge centrality. Our analysis demonstrated a strong relationship and overlap between psychopathological symptom load and functional impairment, especially between cognitive symptoms and functionality. Furthermore, we also observed how abstract thinking relates to hostility and tension.

According to the PANNS and mini-ICF-APP scores, our sample can be considered severely ill [9,15,25]; the CGI-S score further confirmed this [16]. In addition, all patients were hospitalized for treatment; thus, we can generally consider the symptoms and impairment to be clinically relevant, as they can cause a significant burden and impairment. The relationship and agreement between the two scales are high [41], indicating that symptom load and impairment overlap and that a greater symptom load is related to greater degrees of impairment [15]. However, we could not determine whether single symptom domains (neither in the three-factor model nor the five-factor model) were related to greater disability. Interestingly, we did not find an often-described [42,46] correlation between cognitive and negative symptoms and functional impairment. Furthermore, positive and negative symptoms had a lower correlation (although not as pronounced) with the general symptom domain.

The analysis of the PANSS revealed the importance of specific symptoms (N05: Abstract Thinking, G08: Uncooperativeness) in the network; interestingly, those symptoms were strongly related to features (i.e., P07: Hostility and G04: Tension) determining the urgency of treatment. The analysis also revealed the importance of cognitive symptoms (N05: Abstract Thinking, and G12: Lack of Judgment) over purely negative symptoms (e.g., N06: Lack of Spontaneity) or positive symptoms (e.g., P03: Hallucinations). Thus, these findings support the notion that functional impairment is mediated through negative cognitive symptoms [18,32].

Through the identification of bride symptoms, our study revealed that cognitive symptoms impair the ability to adhere to routines (and comply with rules) in the joint network of symptoms and functional domains. The importance of adhering to routines and compliance with regulations seems to be common across individuals with mental disorders and is mediated through difficulties in planning for other functional domains [19,36]. Therefore, alleviating the severity of cognitive symptoms could result in improvements in many other symptoms, making these symptoms primary treatment targets. However, our study cannot reveal causal interactions; thus, future longitudinal studies are needed to determine causality.

There are various treatment approaches (e.g., cognitive behavioral therapy, psychoeducation, social skills training, and cognitive remediation) available to achieve not only adherence but also commitment and engagement with treatment in patients hospitalized with a psychotic disorder, despite the duration of the illness (i.e., first episode or chronic) [1,31]. In pharmacological treatment, the need for regular and routine intake of the medication is recognized, with the result that several antipsychotics are available as long-acting injectables [17,43] that might improve functioning [34].

Another aspect to be considered with respect to adherence to a routine and compliance with rules is cognitive processes that usually allow navigation through daily life and changing conditions. In schizophrenia patients, cognitive capabilities and thought processes are disrupted and related to adherence to routines on the one hand and compliance with rules on the other hand. Furthermore, they are also associated with uncooperative and even hostile behavior. Thus, disorders and cognitive impairment play pivotal roles; other symptom complexes are closely related to these domains [21]. We believe that combined interventions addressing neuropsychological and neurocognitive aspects of this disorder, such as neurocognitive remediation, have great potential to improve other domains of the disorder [12,48].

Our results also show that psychopathology negatively impacts the mobility of patients (mainly through avoidance) [3], thus impeding patients from seeking other forms of treatment, such as ambulatory therapies. We also observed a close relationship between the cognitive thought process and psychotic symptoms. Our results show the importance of a cognitive and valuative system for seeking and maintaining personal and social relationships; this requires mentalization, empathy, and self-confidence [35].

Previous analyses of the relationship between symptoms and psychosocial functioning in patients with schizophrenia have mostly examined these relationships in patients with a first episode of schizophrenia [7,13,14,21]. In contrast, our study analyzed a clinical population with several previous hospitalizations for treatment. Network analysis has been increasingly used to gain a better understanding of the relationships between symptoms, other disorder-related parameters, and functionality in patients with schizophrenia; it provides a layered, comprehensive understanding of the relationships between symptoms and functional domains in schizophrenia patients beyond their first psychotic episode [13,14].

One limitation of our current study is the inclusion of only observer-rated instruments assessing psychopathology and psychosocial functioning without including neurocognitive domains. Additionally, our sample included only patients requiring hospitalization for treatment,

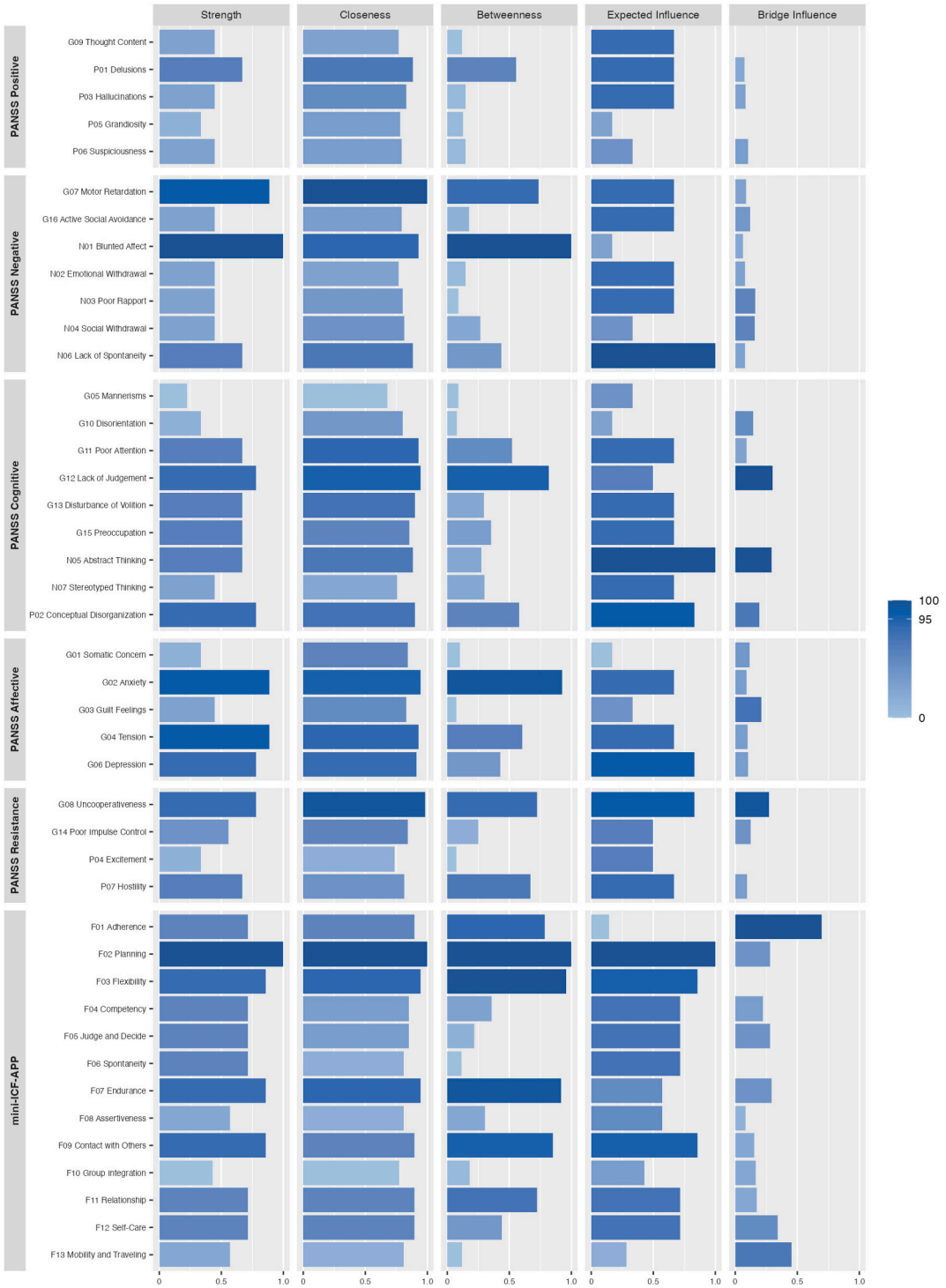

Fig. 2. Network centrality indices of the symptom (PANSS) and psychosocial functionality (mini-ICF-APP) networks.
The initials of the items represent the PANSS three-factor structure, P: Positive; N: Negative; and G: General. The items labeled F belong to the mini-ICF-APP.

which represented those with more severe disease. Since our sample data were derived from routine clinical practice, the details provided can differ from those obtained in controlled trials [45]. In contrast, the requirement for hospitalization underlines the disabling nature of psychopathology [19,38].

In conclusion, owing to the high magnitude of functional impairment in patients with schizophrenia-spectrum disorders, we studied the associations between various items related to psychosocial functioning, as measured with the mini-ICF-APP, and various positive, negative, and general psychopathology symptoms, as assessed with the Positive and Negative Symptom Scale. Our study revealed a strong relationship between symptom load and functional impairment in patients with schizophrenia, beyond any single dimension of the disorder. Furthermore, through the network approach, we could add to the notion that the symptoms and their interactions constitute the disorder beyond the single manifestations of schizophrenia.

We were able to demonstrate the crucial role of adhering to rules and routines for those affected and its role as a target of intervention and

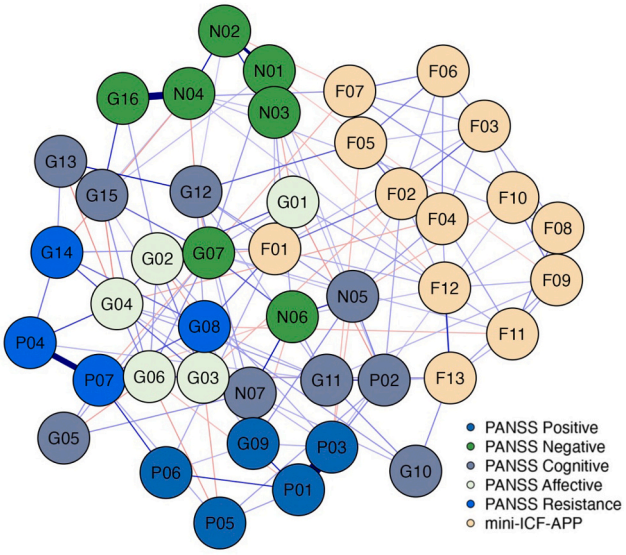

Fig. 3. Network structure of the symptom (PANSS) and psychosocial functionality (mini-ICF-APP) network.
PANSS items are as follows: (The initials of the respective dimensions represent the PANSS three-factor structure, P: Positive; N: Negative; and G: General; the items belonging to the different dimensions of the PANSS five-dimensional structure model are listed below).
Positive dimensions: Item P01: Delusions; Item P03: Hallucinations; Item P05: Grandiosity; Item P06: Suspiciousness; Item G09: Thought Content.
Negative Dimension: Item N01: Blunted Affect; Item N02: Emotional Withdrawal; Item N03: Poor Rapport; Item N04: Social Withdrawal; Item N06: Lack of Spontaneity; Item G07: Motor Retardation; Item G16: Active Social Avoidance.
Cognitive Dimension: Item P02: Conceptual Disorganization; Item N05: Abstract Thinking; Item N07: Stereotyped Thinking. Item G05: Mannerisms; Item G10: Disorientation; Item G11: Poor attention; Item G12: Lack of Judgment: Item G13: Disturbance of Volition; Item G15: Preoccupation.
Affective Dimension: Items G01: Somatic Concern; Item G02: Anxiety; Item G03: Guilt Feelings; Item G04: Tension; Item G06: Depression.
Resistance Dimension: Item P04: Excitement; Item P07: Hostility. Item G08: Uncooperativeness; Item G14: Poor Impulse Control.
mini-ICF-APP Items:
Item F01: Adherence; Item F02: Planning; Item F03: Flexibility; Item F04: Competency; Item F05: Judge and Decide; Item F06: Spontaneity; Item F07: Endurance; Item F08: Assertiveness; Item F09: Contact with Others: Item F10: Group Integration; Item F11: Relationship; Item F12: Self-Care; Item F13: Mobility and Traveling. Within the graphical representation, edges are the lines between the nodes (items) representing regularized partial correlations, which help estimate the relationship between two variables while controlling for all other variables. An edge indicates a dependent relationship between variables; the absence of an edge indicates that the variables are conditionally independent. The blue edges represent positive associations, while the red edges represent negative associations. The wider and more saturated an edge is represented, the stronger the association.

different treatment approaches. We further showed that the interplay between symptoms and functional domains in schizophrenia patients is complex and variable and is mediated mainly by cognitive and thought processes. Therefore, we suggest that cognitive testing should be part of the standard assessment in patients with schizophrenia. Furthermore, general interventions, such as establishing routine or improving cognitive processing (e.g., cognitive training or cognitive remediation), are needed early in the treatment process.

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CRediT authorship contribution statement

Mona Redlich Bossy: Writing – review & editing, Writing – original draft, Data curation. **Daniel R. Müller:** Writing – review & editing, Supervision. **Daryl W. Niedermoser:** Writing – review & editing, Writing – original draft. **Achim Burrer:** Writing – review & editing. **Tobias R. Spiller:** Writing – review & editing, Methodology. **Stefan Vetter:** Writing – review & editing, Supervision, Resources, Project administration, Funding acquisition. **Erich Seifritz:** Writing – review & editing, Supervision, Resources, Methodology. **Stephan T. Egger:** Writing – review & editing, Writing – original draft, Visualization, Software, Project administration, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors have no conflicts of interest to disclose.

Data availability

The data supporting this study's findings are available from the corresponding author, STE, upon reasonable request.

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