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THE BORDERS OF MENTAL ILLNESS: INVESTIGATING CLUSTERS OF DIAGNOSTIC CRITERIA IN ACUTE PRESENTATIONS OF PSYCHIATRIC DISORDERS

Eileen Rogge & Giovanni Briganti

Laboratoire de Psychologie Médicale et Addictologie, CHU Brugmann, Faculty of Medicine, Université libre de Bruxelles, Brussels, Belgium

Chair of Artificial Intelligence and Digital Medicine, Faculty of Medicine, University of Mons, Mons, Belgium

SUMMARY

The impact of diagnostic delay in mental health is significant in terms of neurocognitive impairment, comorbidities, prognostic and socio-economical cost. For this reason, diagnostical research in psychiatry and the classification methods are continuously questioned. The network theory of mental disorders aims at contributing to the improvement of psychiatric diagnosis and considers mental disorders as the results of complex sets of interactions among symptoms instead of being their common cause. In this study, we use network theory and its associate statistical methods, namely Gaussian Graphical Models, centrality, and cluster analysis, to estimate respectively the interactions among symptoms from different disorders, their relative importance, and how they overlap, in a sample of psychiatric inpatients. The community detection found nine clusters with their interactions. Many are closely related to DSM criteria but some of them share symptoms from both diagnostics. One central symptom of the construct is Insomnia. There was a significant difference in the sum scores for psychotic symptoms, but not for bipolar symptoms, across psychotic and bipolar patients. This study needs however to be replicated in a bigger sample of different patients. Computing Bayesian Network to assess causalities in the network and adding other variables (such as biomarkers or therapeutic responses) could contribute to a more personalized diagnostic. How symptoms connect to each other in a specific time frame would define a person phenotype. Network analysis allows for investigating connections, identifying which symptoms are relatively important to the self-determination of disorders as well as how network nodes predict each other and arise in communities. For instance, in psychotic and mood disorders, sleep related symptoms or altered speech features and the importance of their communities in the probable transfer of symptomatology.

Key words: *psychiatry - networks - psychological constructs - psychotic disorders - mood disorders*

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INTRODUCTION

Psychiatric diagnosis has not only an important medical impact on the lives of patients but has significant societal implications (Kornreich 2021). Therefore, research is based on improving the overlapping clinical utility, validity and reliability of classifications (Gaebel 2012). However, medical classifications are overall underperforming in clinical context (Reed et al. 2018). Inaccurate diagnosis can lead to therapeutical delay. In psychosis and mood disorders, this delay significantly increases the neurocognitive impairment, the risk of other comorbidities and poor outcomes after treatment as well as the socio-economical cost (Chen et al. 2020, McCombs et al. 2007).

One of the commonly debated reasons for the poor fit of psychiatric classifications in clinical practice is that psychiatric disorders are conceived as natural kinds, as most medical conditions. An increasing number of medical and behavioral scientists consider psychiatric disorders as the result of the complex set of interactions among symptoms, with specific disorders understood as clusters of symptoms that are more likely than others to co-present in the same time frame (Kendler et al. 2011). This complex approach can be particularly plausible in the case of psychotic and mood disorders as they are known to overlap (Pearlson 2015, Barr et al. 2022).

The network theory is a new framework for the study of the ontology of mental disorders and proposed a decade ago to investigate the complexity of psychopathological processes (Borsboom 2008). This approach models disorders as emerging from interrelated symptoms by computing data, often collected from psychometric scales. Network analysis is the set of statistical tools that stems from the network theory: network structures are estimated as a set of nodes (symptoms) and edges (connections) that allows researcher to investigate the complexity of mental disorders as well as identify highly connected symptoms ("central"), and clusters or "communities" of highly connected symptoms. From a data mining approach, it allows for uncovering uninvestigated properties of mental disorders by studying the way symptoms interact, instead of whole syndromes (Henry et al. 2021).

A number of psychiatric constructs have been investigated through the lens of network analysis, such as psychotic disorders (Moffa et al. 2021) and mood disorders (Briganti et al. 2021a,b, McNally et al. 2022). However, the overlap between the two syndromes has not been investigated from a network perspective, using modern machine learning tools such as community detection. When investigating both psychotic and mood disorders, for instance, the potential overlap may concern both positive symptoms from psychotic

disorders and manic symptoms from mood disorders, as well as negative symptoms and symptoms associated with low mood.

The aim of this study is therefore to investigate the interaction, predictability and overlap among symptoms from psychotic and mood disorders using network analysis, in a sample of patients presenting with a severe clinical presentation. This study is structured as follows. Firstly, we present the methods used to carry out this investigation. Secondly, we present the main results from our analyses. Thirdly, we discuss our findings and their potential limitations.

METHODS

Ethical approval

The protocol for this study was approved by the Ethical Committee of the CHU-Brugmann Hospital in Brussels, Belgium (reference number: CE 2021/58).

Data set. Patients

This is a prospective cohort study. The data set is composed of 101 inpatients in a secure care unit specialized in mood disorders and psychotic disorders, in CHU-Brugmann in Brussels, from February 2021 to February 2022. Patients were included if they were 18 to 78 years old diagnosed with a psychotic (e.g., schizophrenia, schizo-affective disorder, psychosis) or mood disorder (e.g., bipolar disorders, major depressive disorders) following the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) criteria. Blood and urine analysis were realized as part of the early clinical evaluation of patients to exclude an exogen etiology (such as drugs). All patients included were treated with a standard set of drugs following the local protocol.

Measurement

The data were collected from administering psychometric scales during direct interviews patients. Observation are encoded as anonymous in the data set to preserve patient confidentiality.

We used DSM-V (American Psychiatric Association 2013) criteria as well as several verified scales to assess symptoms in each patient at the time of their admission. The scales were: the Bipolar Inventory of Symptoms Scale (BISS 2.1; 2012), the Scale for the assessment of Positive Symptoms (SAPS 2.0; 1995) the Scale for the Assessment of Negative Symptoms (SANS 2.0; 1999).

Network analysis. Software

The software used for statistical computing is Rstudio (version 4.1.1, available at https://www.r-project.org). The packages needed for the analyses were EGAnet (Golino et al. 2020), qgraph (Epskamp et al. 2012), mgm (Haslbeck & Waldorp 2020), glasso (Friedman & Tibshirani 2019), igraph (Csardi & Nepusz 2006), BGGM (Williams & Mulder 2021), NetworkComparisonTest (Borkulo et al. 2019) and bootnet (Epskamp et al. 2018).

Node selection

The presence of redundant items may wrongly influence the importance of a variable since redundant nodes are semantically correlated. Nevertheless, the communities may also be altered.

Node selection has been made at two levels. First, to avoid redundancies. Second, to be statistically significant and compute correctly the Network analysis and inferences and have a best number of studied cases compared to the items assessed. The node selection for the community detection and for network inference is disponible Table 1 and 2.

We used the Unique Variable Analysis (UVA) technique to detect redundancies. This technique evaluates the shared number and intensity of connections of similar connected nodes. All the assessed and accurate redundancies were removed from the data set used for the further assessments.

Table 1. Global node selection for EGA communities detection

Selected Variable	Detected as Redundant
B25: Aggressivity	P23: Aggressivity/ Agitation
B30: Increased sexuality	N18: Decreased sexual activity; B12: Reduced sexual activity
P16: Mindreading delusion	P17: Thought broadcasting delusion
B13: Anxiety reported	B5: Worry
N20: Relationships	B11: Social withdraw; B27: Increased social interest
P11: Grandiosity delusion	B32: Grandiosity
B20: Increased appetite	B19: Reduced appetite
P21: Appearance and clothing	B43: Appearance
P10: Guilt or Sin delusion	B6: Guilt
N22: Social inattention	N23: Inattentiveness; N24: Global attention
P31: Pressure of speech	B29: Pressure of speech
P8: Persecution Delusion	B40: Persecutory ideas
P32: Distractible speech	B37: Distractible
P20: Global Delusion	B41: Delusion or Hallucination

Table 2. Node Selection for inferences

Scales	Selected Variable	Detected as Redundant
BISS	B30: Increased sexuality	B12: Reduced sexual activity
	B13: Anxiety reported	B5: Worry
	B11: Social withdraw	B27: Increased social interest
	B19: Reduced appetite	B20: Increased appetite
	B1: Sadness reported	B2: Sadness observed
	B23: Irritability reported	B24: Irritability observed
SAPS	P16: Mindreading delusion	P17: Thought broadcasting delusion; P18: Thought installation delusion; P19: Thoughts Withdraw delusion
	P1: Auditive hallucinations	P2: Voice commenting; P3: Voice conversing
	/	P7: Global Rating of Hallucinations; P20: Global Rating of Delusions; P25: Global Rating of Bizarre Behavior; P34: Global Rating of Positive Formal Thought Disorder
SANS	N2: Spontaneous Movement	N3: Expressive Gestures
	N22: Social inattention	N23: Inattentiveness
	/	N8: Global Rating of Affective Flattening; N13: Global Rating of Alogia; N17: Global Rating of Avolition/Apathy; N22: Global Rating of Anhedonia/ Asociality; N25: Global Rating of Attention

Network Estimation

Network are graphs composed of nodes (representing in our case items/symptoms) connected by edges (the connections between items). Those edges are represented with a thickness and color saturation that represent the importance of the edge. To compute them we commonly use a partial correlation network, that is Gaussian Graphical Model (Epskamp et al. 2018). Partial correlation are estimated through inverting the variance-covariance matrix of the date as there are considered as conditional probabilities. Regularization may be needed to avoid the presence of spurious data. The Graphical Least Absolute Shrinkage and Selection (GLASSO) procedure is used to obtain this regularized partial correlation network (Friedman & Tibshirani 2019). The Fruchterman-Reignold algorithm is used to place closely connected nodes next to each other (Fruchterman & Reingold 1991).

Network Inference

Community Detection

The walktrapp algorithm was used to identify the communities of items in the graph. It is based on the principle that adjacent nodes tend to belong to the same community (Yang et al. 2016). It has been demonstrated that the walktrapp algorithm has a high accuracy in simulation studies (Demetriou et al. 2017, Golino & Epskamp 2017).

Centrality

Centrality measures allows the identification of nodes interconnections in the network. It can be defined in three indices: betweenness, closeness and strength. The strength centrality is the most relevant for psychopathology and is used in this work (Bringmann et al. 2019). It is the sum of the absolute values of all the connected edges to the node of interest and assesses what is considered as the most central or more connected node of the network. The more central nodes can therefore better predict/be predicted by others and is the most suitable symptoms to target in treatment as it is the one considered having the more influence on the construct (Boccaletti et al. 2006).

Predictability

Predictability is another measure of node connectivity. It is the R^2 estimated for each node in the network based on other nodes. It explores the percentage of a node's variability that can be justified by other nodes' variations (Haslbeck & Waldorp 2020).

Network Comparison test

We use the Network Comparison Test (NCT) to compare our networks structures. It explores the differences in the global connectivity of the structures (Borkulo et al. 2019). The NCT rearranges the samples to test whether two networks are invariant with respect to global strength (sum of all edge weights), network structure and edge values.

RESULTS

Descriptive statistics

In this study, as seen in Table 3, 101 patients have been included with 55% of women and 45% of men. 53 of them were diagnosed with mood disorders with a majority of women (62%) and 48 of them with psychotic disorders with the same distribution in men and women (52% vs 48%). Ages range from 18 to 75 years old with a mean at 43 years old (CI 95% [40.2-45.9], standard deviation at 14.6).

Table 3. Descriptive Statistics for age, sex and diagnostic in each scale

						95% CI					
	Diagnostique	Sex	N	Missing	Mean	Lower	Upper	Median	SD	Minimum	Maximum
Age - all			101	0	43.4	40.5	46.4	46	15.1	18	82
Age	Mood	F	33	0	48.8	43.1	54.4	50	16.6	21	82
		M	20	0	45.0	38.0	52.0	47.5	16.0	21	74
	Psychosis	F	23	0	41.7	36.5	46.8	46	12.6	18	59
		M	25	0	36.8	32.1	41.4	32	11.8	22	57
BISS	Mood	F	33	0	62.0	56.1	67.8	60	17.1	32	110
		M	20	0	59.9	52.2	67.5	62.0	17.5	23	86
	Psychosis	F	23	0	64.1	55.4	72.7	66	21.2	26	117
		M	25	0	59.4	52.1	66.7	57	18.6	17	95
SAPS	Mood	F	33	0	33.8	27.5	40.2	33	18.6	2	67
		M	20	0	28.8	21.2	36.4	28.5	17.4	2	65
	Psychosis	F	23	0	48.5	40.3	56.7	48	20.0	18	100
		M	25	0	46.3	38.2	54.3	45	20.5	15	88
SANS	Mood	F	33	0	30.1	21.7	38.4	23	24.5	1	100
		M	20	0	32.0	24.6	39.5	33.0	17.1	3	63
	Psychosis	F	23	0	44.6	36.5	52.7	44	19.7	2	78
		M	25	0	52.2	41.2	63.3	52	28.2	7	113

Note: 95%CI - 95% Confidence Interval

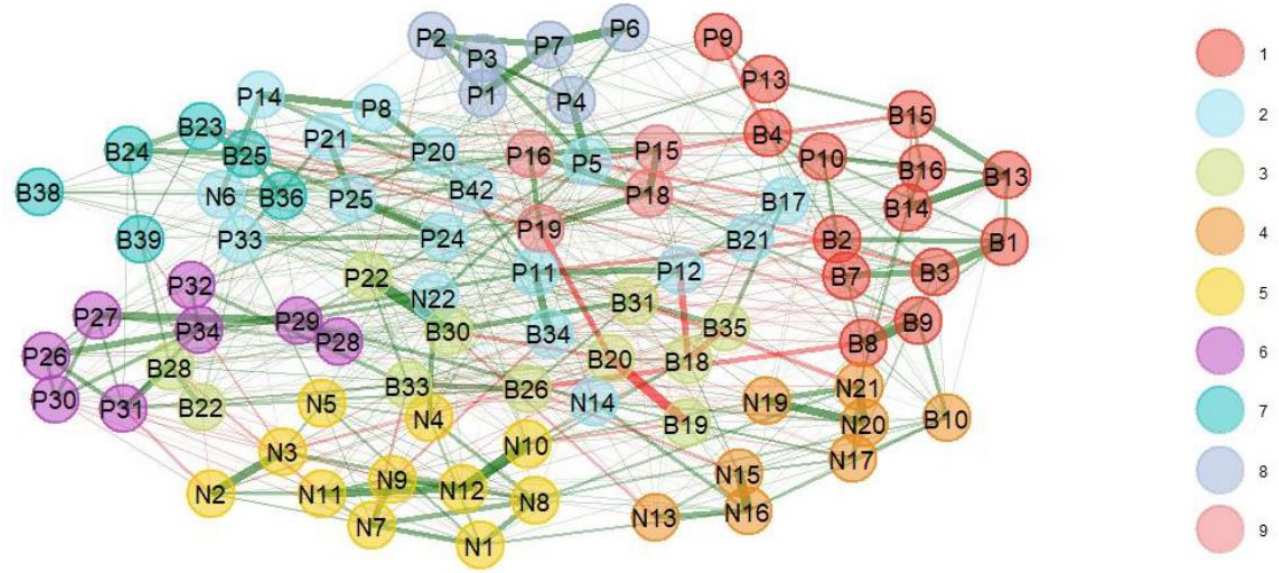

Figure 1. EGA global network and community detection of psychotic and mood disorders

Network estimation and community detection

EGA network

In this EGA (exploratory graph analysis), Figure 1, nine communities are detected. They have been called by the main items composing them: "Depressed mood and anxiety", "Insomnia, cognitive impairment and inappropriate behavior", "Decreased need of sleep and agitated state", "Anhedonia, anergia, abulia", "Inexpression", "Disorganized and altered speech", "Irritability and emotional lability", "Hallucinations", "Control delusions". All of them are detailed Table 4.

As shown by edges in Figure 1, partial correlations have been detected between the items within the communities but also between items from different community. Some of them are discussed later. The details of all edges are available in Table 5.

Network inferences

Centrality

In Figures 2a to 2c, centralities are represented for each scales. In the BISS, the most central symptom is "Insomnia" (centrality (c): 4,65), close to "Impulsivity" (c: 4,58), "Racing thoughts"(c: 4,54) and "Delusion of guilt"(c: 4,52). In the SAPS, the most central nodes are the symptoms "Pressure of speech" (c: 3,64) and "Auditive hallucinations" (c: 3,62). For the SANS, "Blocking in speech" is the most interconnected node (c: 2,64) with "Unability to feel intimacy or closeness" (c: 2,55), "Lack of vocal inflection" (c: 2,5).

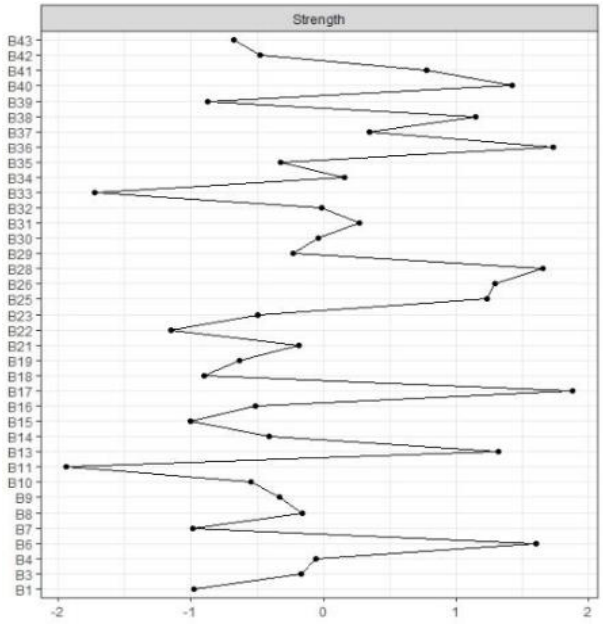

Figure 2a. Centrality of BISS items

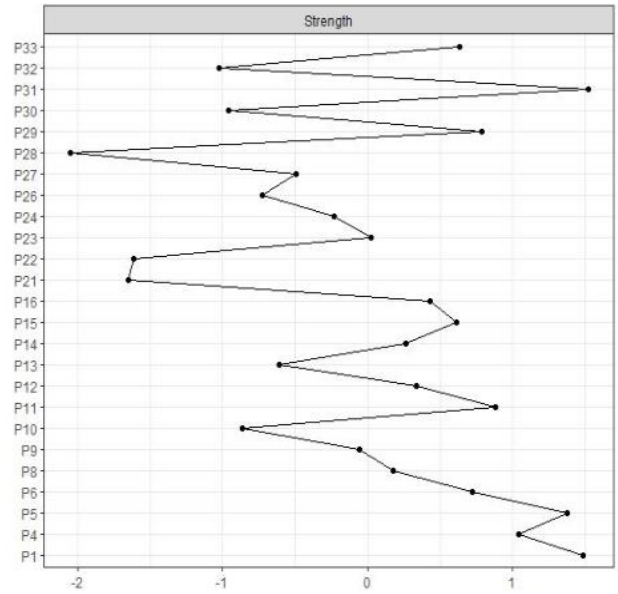

Figure 2b. Centrality of SAPS items

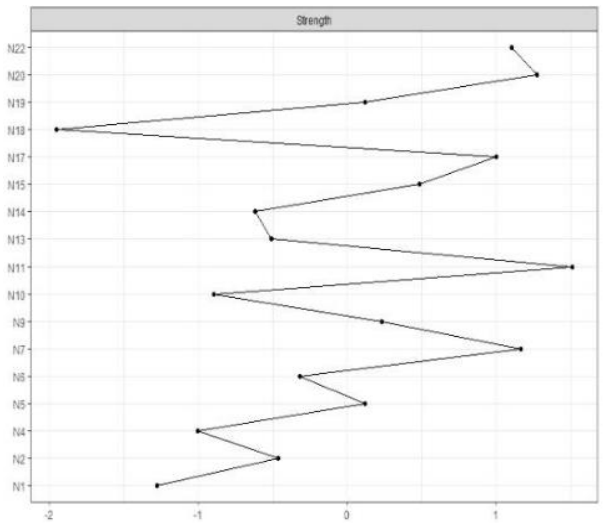

Figure 2c. Centrality of SANS items

Table 4. Communities from EGA community detection

Name of Communities Item	Item's name
Depressed mood and anxiety	
B1	Sadness Reported
B2	Sadness Observed
B3	Pessimism
B4	Suicidality
B7	Feeling of Inadequacy
B8	Low Energy
B9	Psychomotor Slowing
B13	Anxiety Reported
B14	Anxiety Observed
B15	Somatic Anxiety-Reported
B16	Fearfulness
P9	Delusion of Jealousy
P10	Delusion of Guilt
Insomnia, cognitive impairment and Inappropriate behavior	
B17	Insomnia
B21	Impaired Concentration
B34	Sharpened Thinking
B42	Impaired Insight
P5	Olfactory Hallucination
P8	Persecutory Delusion
P11	Grandiose Delusion
P12	Religious Delusion
P14	Delusion of Reference
P20	Global rating of Delusion
P21	Clothing and Appearance
P24	Repetitive and Stereotyped Behavior
P25	Global rating of Bizarre Behavior
P33	Clanging
N6	Inappropriate Affect
N14	Grooming and Hygiene
N22	Global Rating of Anhedonia/Asociality
Decreased need of sleep and agitated state	
B18	Excessive sleep
B19	Reduced Appetite
B20	Increased Appetite
B22	Agitation
B26	Energetic
B28	Racing Thoughts-Reported
B30	Increased Sexuality
B31	Less Need for Sleep
B33	Elated
B35	Elevated Evening Energy or Interest
P22	Social and Sexual Behavior
Anhedonia, anergia, abulia	
B10	Loss of interest
N13	Global Rating of Alogia
N15	Impersistence at work or school
N16	Physical Anergia
N17	Global rating of Avolition/Apathy
N19	Sexual Activity
N20	Ability to feel Intimacy and Closeness
N21	Relationships with Friends and Peers

Table 4. Continues

Name of Communities Item	Item's name
Inexpression	
N1	Unchanging Facial Expression
N2	Decreased Spontaneous Movement
N3	Paucity of Expressive Gestures
N4	Poor Eye Contact
N5	Affective Unresponsivity
N7	Lack of Vocal Inflections
N8	Global Rating of Affective Flattening
N9	Poverty of Speech
N10	Poverty of Content of Speech
N11	Blocking
N12	Increase Latency of response
Disorganized and Altered speech	
P26	Derailment
P27	Tangentiality
P28	Incoherence
P29	Illogicality
P30	Circumstantiality
P31	Pressure of speech
P32	Distractible speech
P34	Global rating of positive formal thought
Irritability and Emotionality lability	
B23	Irritability reported
B24	Irritability observed
B25	Aggressive behavior
B36	Impulsivity
B38	Risky behavior
B39	Affective lability
Hallucination	
P1	Auditive
P2	Voice Commenting
P3	Voice Conversing
P4	Somatic or Tactile
P6	Olfactory
P7	Global rate of Hallucination
Control Delusion	
P15	Delusions of Being Controlled
P16	Delusions of Mind Reading
P18	Thought Broadcasting
P19	Thought Withdrawal

Predictability

The mean predictability for nodes in the BISS, SAPS and SANS scales are respectively 46%, 40% and 53%. For the BISS, "Pressure of speech" (Predictability (P): 0,705) and "Energetic" (P: 0,744) are the most predictable followed by "Racing thoughts" (P: 0,701) and "Low Energy" (P: 0,693). In the SAPS, "Somatic/Tactile Hallucination"(P: 0,679) and again "Pressure of speech" (P:0,67) are the most predictable. In the SANS, "Blocking in speech" (P: 0,764), "Lack of vocal inflection" (P: 0,76) are the most predictable, followed by "Poverty of speech" (P: 0,723) and "Inability to feel intimacy or closeness" (P: 0,726).

Network comparison

Independent tests

The independent Student t test in Table 6, shows that there was a difference between the two groups for the SAPS and the SANS (p<0.001) but not for the BISS (p=0.939).

NCT : Network comparison test

For all scales, no difference in global edge weights and global strength between the two groups was detected. P-values of NCT is available in Table 7.

DISCUSSION

To our knowledge, this is the first study associating symptoms from psychotic and mood disorders in a population of psychiatric inpatients with severe clinical presentations. The important goal of this study was to investigate how symptoms from both spectrums connect, and whether they merge into interconnected communities. Community detection, while a machine learning technique, can have important clinical implications: as communities are detected from population level partial correlation matrix, networks are known to replicate well within individual (Klipstein et al. 2021): cross-sectional psychopathological network therefore have an important exploratory added value as they can define which other symptoms are more likely to present at the same time in individuals that have a given symptom, i.e., describing data-driven phenotypes for mental disorders. This is especially important at the cross-roads of psychotic and mood disorders, which have long been known to overlap (Pearlson 2015).

Community detection showed that many clusters of items are from the same scale, which is of course to be expected: it means that symptoms from a same scale pathology tend to be closely related to each other based on the DSM-V criteria (American Psychiatric Association 2013). We compared DSM criteria and communities in Table 8. Some communities however share symptoms from both psychotic and mood disorders. This is the case for several communities in our network. For example, a patient with negative symptoms may present either symptoms related to anhedonia (such as loss of interest) and inability to feel close, or related to inexpression and poverty of speech and affect. In more, the second community detected in the EGA network is gathering items from every scales. It is the cluster composed of insomnia, cognitive and delusion features as well as inappropriate behaviors. It is one of the most interconnected communities along with the "Decreased need of sleep and agitated state" and the "Depressed mood and anxiety" clusters. These can be understood as the clusters that best transfer information to the rest of the network: as they contribute to the self-determination of the network (how the network is constructed), this implies that they could eventually be good targets for improving therapeutic intervention.

Table 5. Partial Correlations between symptoms from the EGA network

Community	Correlation's items	Correlation's name	Correlation's coefficient
1: Depressed mood and Anxiety	B9-B8	Low Energy - Psychomotor slowing	0.807
	B1-B2	Sadness reported – Sadness observed	0.712
	B13-B14	Anxiety reported – Anxiety observed	0.697
	B3-B7	Pessimism - Feeling of Inadequacy	0.682
	B13-B15	Anxiety reported - Somatic Anxiety reported	0.608
	B16-P10	Fearfulness - Delusion of Guilt	0.559
2: Insomnia, cognitive impairment and inappropriate behavior	P11-B34	Grandiose Delusions - Sharpened Thinking	0.754
	P8-14	Persecutory delusion - Delusion of reference	0.617
	P11-12	Grandiose Delusion - Religious Delusion	0.588
	P25-24	Repetitive and Agitated behavior - Global rating of Bizarre Behavior	0.570
	P25-P21	Clothing and Appearance - Global rating of bizarre behavior	0.522
	P14-N6	Delusion of reference - inappropriate affect	0.503
	P33-P24	Repetitive and Agitated behavior - Clanging	0.449
3: Decreased need of sleep and agitated state	B33-B26	Elated - Energetic	0.829
	P22-B30	Social and Sexual Behavior - Increased sexuality	0.73
	B18-B35	Excessive sleep - Elevated evening energy, interest	-0.653
	B20-B19	Reduced appetite - Increased appetite	-0.594
4: Anhedonia, anergia, abulia	N15-N16	Impersistence at work or school - Physical anergia	0.892
	N19-N20	Sexual activity - Ability to feel intimacy and closeness	0.791
5: Inexpression	N11-N12	Blocking - Increased latency of response	0.854
	N2-N3	Decreased spontaneous movement - Poverty of expressive gestures	0.846
	N10-N12	Poverty of content of speech - Increased latency of response	0.843
6: Disorganized and altered speech	P26-P34	Derailment - Global rating of positive formal thought	0.797
	P28-P29	Incoherence - Illogicality	0.736
	P27-29	Tangentiality - Illogicality	0.682
7: Irritability and emotional lability	B23-B25	Irritability reported - Aggressive behavior	0.586
	B24-B25	Irritability observed - Aggressive behavior	0.566
8: Hallucination	P1-P7	Auditory hallucination - Global rating hallucination	0.822
	P6-P7	Visual hallucination - Global rating hallucination	0.793
	P2-P7	Voice commenting - Global rating hallucination	0.789
9: Control Delusion	P15-P18	Delusions of Being Controlled - Thought Broadcasting	0.775
	P18-P16	Thought Broadcasting - Delusions of Mind Reading	0.746
	P18-P19	Thought Broadcasting - Thought Withdrawal	0.722
	P15-P16	Delusions of Being Controlled - Delusions of Mind Reading	0.705
	P19-P16	Thought Withdrawal - Delusions of Mind Reading	0.687

Table 5. Continues

Interconnections	Correlation's items	Correlation's name	Correlation's coefficient
1: Depressed mood and anxiety – 3: Decreased need of sleep and agitated state	*B8-B26*	*Low Energy - Energetic*	*-0.759*
1: Depressed mood and anxiety – 4: Anhedonia, anergia, abulia	*B9-B10*	*Psychomotor Slowing – Lost of interest*	*0.660*
1: Depressed mood and anxiety – 9: Control delusion	B4-P15	Suicidality - Delusions of being controlled	-0.131
2: Insomnia, cognitive impairment and inappropriate behavior – 3: Decreased need of sleep ad agitated state	P12-B18	Religious Delusion - Excessive sleep	-0.499
2: Insomnia, cognitive impairment and inappropriate behavior – 6: Disorganized and altered speech	*P11-P34*	*Grandiose Delusions – Global Rating of positive formal thought*	*0.700*
2: Insomnia, cognitive impairment and inappropriate behavior – 6: Disorganized and altered speech	N22-P29	Global Rating of Anhedonia/Asociality – Illogicality	0.530
2: Insomnia, cognitive impairment and inappropriate behavior – 8: Hallucinations	*P5-P4*	*Olfactory hallucinations - Somatic or Tactile hallucinations*	*0.722*
2: Insomnia, cognitive impairment and inappropriate behavior – 8: Hallucination	P5-P3	Olfactory hallucination - Voice conversing Hallucination	0.656
3: Decreased need of sleep and agitated state – 6: Disorganized and altered speech	B33-P32	Elated – Distractible Speech	0.530
3: Decreased need of sleep and agitated state – 9: Control Delusions	B20-P19	Increased Appetite -Thought Withdrawal	-0.536

Table 6. Independent test assessing the difference between psychotic and mood disorders diagnostic in each scale

							95%CI			
		Statistics	df	p	M. diff.	SE difference	Lower	Upper		Effect Size
BISS	Student's t	-0.135	99.0	0.893	-0.497	3.67	-7.79	6.79	Cohen's d	-0.0269
SAPS	Student's t	-4.051	99.0	<0.001	-15.409	3.80	-22.96	-7.86	Cohen's d	-0.8072
SANS	Student's t	-3.848	99.0	<0.001	-17.753	4.61	-26.91	-8.60	Cohen's d	-0.7667

Note: 95%CI - 95% Confidence Interval; M. diff. - Mean difference

Table 7. p-values resulting from the Network Comparison Test

	p-values	
	Edge weights	Global strength
BISS	1	1
SAPS	1	1
SANS	1	1

Edge weights p value is the one resulting from the permutation test concerning the maximum difference in edge weights. Global strength p value is the one resulting from the permutation test concerning difference in global strength

Overall, communities with negative symptoms and emotional lability interact less with the rest of the network. The negative symptoms that are shared between psychotic and mood disorders are likely to share information between psychotic negative symptoms and the symptoms from bipolar depression. For instance, there is a negative influence between excessive sleep and religious delusion but also a connection between fearfulness (connected with anxiety) and delusion of guilt (connected with sadness or suicidality) are noticed. The latest relation has already been detected in child development (Kochanska et al. 2002).

Among highly connected nodes (with high centrality and predictability estimates), we have the presence of "Altered speech" features in both positive and negative clusters. "Inability to feel intimacy or closeness" is central in the anhedonia cluster, which is a factor of vulnerability to major depression (Loas 1996) and

Table 8. DSM-V criteria and Detected EGA communities comparison

Diagnostic	DSM criteria	Study Results	
		C. num	Name of the community
Schizophrenia			
	Delusions	2 + 9	Insomnia, cognitive impairment and inappropriate behavior + Control Delusion
	Hallucinations	8	Hallucinations
	Disorganized Speech	6	Disorganized and altered speech
	Disorganized Behavior / Catatonia	2 + 5	Insomnia, cognitive impairment and inappropriate behavior + Inexpression
	Negative Symptoms	4 + 5	Anhedonia, anergia, abulia + Inexpression
Mania			
	Grandiosity	2	Insomnia, cognitive impairment and inappropriate behavior
	Decreased need of sleep Increased interest in activity, social activity, sexuality Psychomotor agitation Elated High energy	3	Decreased need of sleep and agitated state
	Pressure of speech Flight of ideas Racing thoughts Distractibility	6	Disorganized and altered speech
	Risky behavior	7	Irritability and emotionality lability
Depression			
	Depressed mood Fatigue/ Low energy Worthlessness/Guilt Suicidality	1	Depressed mood and anxiety
	Agitation or Retardation	3 or 1	Decreased need sleep and agitated state OR Depressed mood and anxiety
	Concentration	2	Insomnia, cognitive impairment and inappropriate behavior
	Loss of weight	3	Decreased need of sleep and agitated state
	Loss of interest	4	Anhedonia, anergia, abulia
	Insomnia or Hypersomnia	2 or 3	Insomnia, cognitive impairment and inappropriate behavior OR Decreased need of sleep and agitated state

Note: C. num - Community number

suicidality (Ducasse et al. 2018) but also as a trans-diagnostic symptom between disorders (Guineau et al. 2022). However, "Anhedonia" and "Depressed mood" are, as a reminder, distinct phenotype linked, for example among other smaller edges, by the connection between Psychomotor slowing and Loss of interest.

Insomnia is the most central node for the BISS. It is thus a key symptom in highly dynamic or heterogenous presentation of pathology. Sleep has been recognized as an important and interconnected symptoms in both psychotic and mood disorders, as shown in other recent studies (McNally et al. 2022, Meyer et al. 2020, Zaks et al. 2022). In our network, insomnia is implied in cognitive and energy loss clusters while the decreased need of sleep is connected to energetic and agitated state. A bridge between the two clusters is the edge shared between Religious Delusion and Excessive sleep.

In our analysis, there was a significant difference in the sum scores for psychotic symptoms, but not for bipolar symptoms, across psychotic and bipolar patients. Some studies assessed that both, positive/manic symptoms and negative/depressive symptoms, are retrieved in the two populations (Kuipers et al. 2019, Pearlson 2015). However, the network structures were not different in the two populations.

The results of this study should be met with a few limitations: we describe three of them. First, the network needs to be replicated in other and bigger samples. Second, we estimated our models in patients with severe presentations: future studies may endeavor to analyze less severe patients and explore whether our results replicate. Third, causal connections were not explored in our sample: future studies may endeavor to use Bayesian Networks to explore the plausible causal connections as well as temporal networks to study

Granger-causal connections. One could introduce variables outside the behavioral spectrum, such as brain regions and biomarkers in the constructs or even the responses to treatment into temporal dynamical networks. These models are likely to contribute to more personalized approaches of psychiatric symptomatology.

CONCLUSION

Network analysis allows some observations that support the interest of complex approach in mental disorders, as symptoms of psychotic and mood disorders share several connections. Network analysis allows for investigating such connections, as well as identifying which symptoms are relatively important to the self-determination of disorders as well as how network nodes predict each other and arise in communities. For instance, in psychotic and mood disorders, sleep related symptoms or altered speech features and the importance of their communities in the probable transfer of symptomatology.

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Contribution of individual authors:

Eileen Rogge: conceived the manuscript, collected the data, performed the statistical analysis, and wrote the manuscript

Giovanni Briganti: designed the study and reviewed the manuscript.

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Correspondence:

Eileen Rogge, MD
Laboratoire de Psychologie Médicale et Addictologie, CHU Brugmann,
Faculty of Medicine, Université libre de Bruxelles
Brussels, Belgium
E-mail: Eileen.Rogge@ulb.be