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Comorbidity among depression, anxiety and stress symptoms in naturalistic clinical samples: A cross-cultural network analysis

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Abstract

Comorbidity between depression and anxiety is well-established across various settings and cultures. We approached comorbidity from the network psychopathology perspective and examined the depression, anxiety/autonomic arousal and stress/tension symptoms in naturalistic clinical samples from Serbia, Italy and Croatia. This was a multisite study in which regularized partial correlation networks of the symptoms, obtained via self-reports on the Depression Anxiety and Stress Scales-21 (DASS-21) in three cross-cultural, clinical samples (total $N = 874$), were compared with respect to centrality, edge weights, community structure and bridge centrality. A moderate degree of similarity in a number of network indices across the three networks was observed. While negative mood emerged to be the most central node, stress/tension nodes were the most likely bridge symptoms between depressive and anxiety/autonomic arousal symptoms. We demonstrated that the network structure and features in mixed clinical samples were similar across three different languages and cultures. The symptoms such as agitation, restlessness and inability to relax functioned as bridges across the three symptom communities explored in this study. Important theoretical and clinical implications were derived.

KEYWORDS

anxiety, clinical samples, comorbidity, depression, network analysis, stress

1 | INTRODUCTION

Comorbidity between depression and anxiety is a well-established phenomenon found across various settings, such as population-representative surveys, primary care and outpatient settings (Dold et al., 2017; Hirschfeld, 2001; Kessler et al., 2015). The presence of comorbid anxiety and depression is associated with a number of important clinical features, namely, greater functional impairment, treatment resistance, premature treatment termination, suicidality and decreased quality of life (Chen et al., 2020; Seo et al., 2011; Young et al., 2006). Hence, a greater understanding of the interplay among anxiety and depression symptoms could help reduce the burden associated with the comorbidity of these two conditions.

Until recently, the prevailing explanation for comorbidity has been the so-called common cause hypothesis, according to which both depression and anxiety symptoms share a common underlying factor, be it genetic, psychological and/or environmental. For example, according to the tripartite model, covariation between depression and anxiety is due to a shared common, latent factor called negative affectivity (NA; Clark & Watson, 1991).

More recently, the network theory of psychopathology has been proposed as an alternative conceptualization (Borsboom, 2017; Cramer et al., 2010). According to this theory, mental disorders are

intertwined networks of symptoms that are mutually reinforcing and causally related to one another. Moreover, some symptoms within the network may have stronger connections than the rest of the network, forming so-called network communities (Golino & Epskamp, 2017). It is worth stressing that comorbidity may stem from symptoms that are shared or overlapping across different disorders (Cramer et al., 2010), in that specific symptoms could not be segregated within a network (or community), but also linked with other networks (or communities). Hence, the activation of shared symptoms could spread from one network and activate symptoms within another network, therefore increasing the risk of comorbidity. Shared symptoms are called bridge symptoms (Cramer et al., 2010), and they have been defined as symptoms within one network community that have the strongest connections with the symptoms belonging to another network community (Jones et al., 2021).

There have been several cross-sectional network studies aiming to improve our understanding of the comorbidity between depression and anxiety (Contreras et al., 2019; Wichers et al., 2021). For instance, Beard et al.'s (2016) study explored the co-presence of depression and anxiety symptoms within a mixed, large clinical sample from the United States, reporting that *Moving or speaking slowly/restless* from the depression network and *Restless* from the anxiety network were the bridge symptoms. Subsequent studies showed that the symptoms of restlessness/agitation/nervous energy acted as bridges across samples and cultures (Kaiser et al., 2021; Wang et al., 2020). Differently from the previous studies, Garabiles et al. (2019), on a sample of Filipino migrants to China, supported the role of *Fatigue*, *Sadness* and *Anhedonia* as important bridges with anxiety symptoms.

In the majority of studies exploring comorbidity, the depression and anxiety symptoms were measured with self-reports reflecting the DSM-IV diagnostic criteria for depression and generalized anxiety disorder (GAD). However, depression is comorbid not only with GAD but also with other anxiety disorders such as panic disorder as well as specific and social phobias (Kessler et al., 1996), that is, disorders that are characterized more by anxious arousal than tension and restlessness (Watson, 2005). Additionally, different anxiety disorders also tend to co-occur in the same individuals (APA, 2013; Watson, 2009). Hence, it would be important to examine a broader array of anxiety symptoms, their mutual relations and their interplay with depression symptoms. A viable instrument for this purpose is the Depression Anxiety and Stress Scales (DASS; Lovibond & Lovibond, 1995) and, in particular, its short version DASS-21 (Henry & Crawford, 2005). Its Depression scale corresponds closely to the DSM-IV criteria for major depression, the Anxiety scale covers criteria for panic disorder and other anxiety disorders characterized by marked fear arousal, while the Stress scale reflects in large part the criteria for GAD.[1] It is important, however, to mention that the DASS-21 was developed without close alignment with any diagnostic system. This characteristic represents an added value for the instrument, given the impact of Berkson's bias identified in many psychological networks (de Ron et al., 2021).

[1](http://www2.psy.unsw.edu.au/dass/DASSFAQ).

Key Practitioners Message

- The DASS-21 can assess the networks of depression, anxiety and stress symptoms in clinical samples in different cultures
- Serbian, Italian and Croatian symptom networks are similar.
- Negative mood is the most central node.
- Stress/tension nodes are the bridges between depressive and anxiety symptoms, suggesting that the stress symptoms might be good intervention targets

The DASS-21 has been translated into many languages (Lovibond, 2017), with a preponderance of validation studies conducted on non-clinical samples (Chin et al., 2019; Osman et al., 2012; Szabó, 2010.), and a few studies on clinical samples (Antony et al., 1998; Bottesi et al., 2015; Clara et al., 2001; Ivezic et al., 2012; Mihić et al., 2021). All validation studies were conducted from the common cause perspective, identifying different possible patterns of latent factors (Bottesi et al., 2015; Mihić et al., 2021). The network approach could provide a different angle from which to consider item covariations whereby the depression, anxiety and stress symptoms hang together due to the dynamic interplay among them, not due to the presence of an underlying factor(s). Moreover, the presence of many translations allows for a cross-cultural comparison of its internal structure.

To the best of our knowledge, there is only one published network study regarding the symptoms of depression, anxiety/autonomic arousal and stress/tension using the DASS-21 on a large, nonclinical, online, international, English-speaking sample (Van den Bergh et al., 2021). The authors reported that *Worthlessness* and *Worried about panic* were the strongest bridges between the depression and autonomic arousal networks. *Down-hearted*, *Lack of initiative*, *Difficulty to relax* and *Agitation* were the symptoms possibly responsible for spreading activation between the depression and stress/tension communities. Finally, *Nervous energy*, *Overreactivity* and *Difficulty to relax*, all from the stress/tension community, could trigger the spreading activation to the anxiety/autonomic arousal community. The authors also found that *Panic* was the most central symptom, followed closely by *Anhedonia*.

Given that Van den Bergh et al.'s (2021) study was the only one to use the DASS-21 to explore comorbidity, additional studies are needed. In particular, it would be highly valuable to explore the structure of depression and anxiety comorbidity within clinical samples, because bridge symptoms, if there are any, are likely to be discovered within the samples experiencing a significant amount of distress (e.g., Boschloo et al., 2015).

Besides there have been some concerns regarding the replicability and generalizability of the psychopathological networks (e.g., Borsboom et al., 2017; Forbes et al., 2017). To the best of our

knowledge, there are only three published network studies using multiple samples, belonging to different cultural/language contexts, with the explicit aim to explore the issues of replicability and generalizability, but none dealt with the depression–anxiety comorbidity issue (de la Torre-Luque et al., 2020; Fonseca-Pedrero et al., 2018; Fried et al., 2018).

Finally, an abundant literature points to cultural variations in prevalence, expression and symptom profiles of depression and anxiety, even among the countries which are in close geographical proximity (e.g., Bernert et al., 2009; Hofmann & Hinton, 2014; Kirmayer, 2001). The sources of these differences might include measurement issues (Simon et al., 2002), problematic diagnostic validity, but also true differences that could stem from genetic liability (Moskvina et al., 2010), socio-economic factors (Weissman et al., 1996), and different cultural values reflecting the extent to which people within society tend to pursue the values that are self-promoting as opposed to those benefiting the collective (Hofstede, 1980; Schwartz, 2006). For example, it has been shown that individualism versus collectivism (Hofstede, 1980) or autonomy versus embeddedness (Schwartz, 2006) are related to the prevalence of common mental disorders (Fischer & Boer, 2011; Heim et al., 2017; van Hemert et al., 2002), and to cognitive vulnerability to depression (Bartucz et al., 2022). Similarly, cultural variation has been associated with different levels of stigmatizing attitudes toward mental health treatment and, in turn, help-seeking behavior (Mojtabai, 2010).

2 | THE PRESENT STUDY

The main aim of the current study was to compare the networks of depression, anxiety/autonomic arousal and stress/tension symptoms in clinical samples from three different countries (Serbia, Croatia and Italy) on a number of network indices: centrality, community structure and edge weights. Serbia, Croatia and Italy are European countries that differ in their level of individualism, with Italy being the highest on this dimension (https://hi.hofstede-insights.com/national-culture). Thus, this scenario represents an interesting opportunity to compare if and how different cultural contexts may affect the structure of depressive, anxiety, and stress symptoms in psychiatric patients. Additionally, we wanted to investigate which particular anxiety/autonomic arousal and stress/tension symptoms were the 'bridges', that is, more connected with particular depression symptoms than others.

Participants were all psychiatric patients (in- or out-patients) who completed the DASS-21. It is important to note that all participants filled out the validated versions of the DASS-21 in their native language (Bottesi et al., 2015; Ivezic et al., 2012; Mihić et al., 2021). By doing so, we were also able to explore potential cross-cultural differences among these three countries regarding the network characteristics of depression, anxiety and stress symptoms. Even though there is abundant literature regarding cultural variations in clinical presentations of depression and anxiety (e.g., Hofmann & Hinton, 2014; Kirmayer, 2001), such variations have been rarely investigated in the context of the network approach to psychopathology and among culturally different countries.

3 | METHODS

3.1 | Study settings and participants

Participants were recruited across different cities in Italy, Serbia and Croatia before the COVID-19 pandemic. In each country, the study was approved by respective ethical committees. All participants signed informed consents and the study was conducted in accordance with the Declaration of Helsinki. This study was based on secondary data sets collected for the validation of the DASS-21 and other instruments (Bottesi et al., 2015; Ivezic et al., 2012; Marčinko et al., 2020; Mihić et al., 2021). A part of the Italian data was collected in the context of broader and currently unpublished projects.

Table 1 provides a summary of the demographic and diagnostic characteristics of the three clinical samples.

3.2 | Measures

The Depression Anxiety and Stress Scales-21 (DASS-21; Bottesi et al., 2015; Henry & Crawford, 2005; Ivezic et al., 2012; Jovanović et al., 2014) is a self-report measure that assesses the symptoms of depression, physiological arousal and tension during the past week, using a 4-point Likert scale. Its good psychometric properties have been reported in the respective national studies.

3.3 | Data analysis

3.3.1 | Data preparation

Initial data consisted of 265 psychiatric patients from Italy, 321 from Croatia and 303 from Serbia. After the exclusion of incomplete cases and multivariate outliers, the final samples were $n_{Ita} = 233$, $n_{Cro} = 299$ and $n_{Ser} = 252$.

3.3.2 | Network estimation

Regularized partial correlation networks were fitted using EBICglasso regularization via 'bootnet' R package (Epskamp et al., 2017; R Core Team, 2019). The networks were estimated using the EstimateNetwork function with default = 'EBICglasso' argument, as a wrapper for the 'EBICglasso' function from the 'qgraph' package (Epskamp et al., 2012), using default settings of the tuning parameter (gamma = .5). Due to deviation from multivariate normality, network

TABLE 1 Characteristics of the three clinical samples.

	N	Males (%)	Mean age (*SD*)	Mean years of education	Exclusion criteria	Diagnoses
Italian sample	265	41.5	38.26 (12.96)	12.00	<18 years old; current or past schizophrenia spectrum or other psychotic disorder; acute manic episodes; major neurocognitive disorder; intellectual disabilities	DSM-5 Substance use disorder (33.6%), borderline personality disorder (21.9%), depressive disorders (14.3%), anorexia nervosa (11.7%), anxiety disorders (10.2%), bulimia nervosa (4.9%), other specified feeding and eating disorder (1.9%), binge-eating disorder (1.5%)
Serbian sample	288	36.8	49.90 (11.20)	12.33	Psychosis, mental retardation; dementia	ICD-10 Depressive episode (37%), recurrent depressive disorder (38%), dysthymia (3%), unspecified affective disorder (4%), brief depressive adjustment reaction (1%), prolonged depressive adjustment reaction (1%), mixed anxiety and depressive reaction (5%), BPD—depression (12%)
Croatian sample	321	39	38.67 (12.08)	13.15	Neurological disorder; acute psychotic disorder; mental retardation/low comprehension skills	ICD-10 Depressive disorders (29%), anxiety disorders (24%), PTSD (15%), adjustment disorder (12%), eating disorders (9%), psychoactive substance use disorders (7%), BPD (4%)

models were based on the Spearman rank correlations. Strength, namely, the sum of the absolute values of the edge weights connected to a node, and expected influence, namely, the sum of the actual values of the edge weights connected to a node, were computed as centrality indicators. Given the very high correlations between these two indices ($r \geq .98$) in the three samples, we compared the networks using the strength index. We also computed the predictability of the nodes in the form of R^2 (Haslbeck & Waldorp, 2020), which represents the variance of a node explained by all its neighbors. To meaningfully compare centrality indices between networks their coefficients of stability should be higher than .25, preferably higher than .50. In our data, strength, expected influences and edge centrality fulfilled these criteria (Table S1 and Figure S1).

3.3.3 | Network communities and bridges

To investigate DASS-21 communities we used three algorithms: walktrap, spinglass and optimal (see Csardi & Nepusz, 2006, and Yang et al., 2016, for more details) from the 'igraph' package (Csardi & Nepusz, 2006). The walktrap algorithm was implemented with three steps of random walks. Since the spinglass algorithm is non-deterministic, the analysis was repeated 1000 times, and we selected the median number of communities as the most appropriate solution. Every time the algorithm was run with the default settings. Detecting communities with the optimal algorithm also used default settings. While determining the number of communities, we searched for correspondence among the different algorithms. The bridge centralities were estimated in R using 'bridge' function from the 'networktools' package (Jones, 2019) with default settings. We reported the bridge strength centrality index given that it is considered the best among other indices (Jones, 2019). The stability of the bridge strength centrality was determined using a bootstrapping procedure with 1000 bootstrap samples, available in 'bootnet' package (Epskamp et al., 2017).

3.3.4 | Network comparisons

We compared the networks in several ways. We correlated edge weights across the networks to obtain indicators of similarity. Network differences were also examined using the network comparison test (Van Borkulo et al., 2022), implemented in R package 'NetworkComparisonTest'. The NCT function provides the omnibus test of network differences and the test of overall network strength differences. Significant omnibus tests were followed by an exploration of differences between individual edge weights in different networks, using 'fdr' correction. Given that NCT does not provide any measure of uncertainty for the observed edge differences, we employed the Bayesian approach and the posterior predictive check test of network

TABLE 2 Means and standard deviations of the DASS-21 items in the three samples.

	Italy				Croatia				Serbia			
Symptom	Mean	*SD*	Sk	Ku	Mean	*SD*	Sk	Ku	Mean	*SD*	Sk	Ku
Hard to wind down	1.37	0.96	−0.92	−0.92	1.32	1.05	0.24	−1.16	1.49	0.94	−0.01	−0.90
Dry mouth	1.15	1.00	−0.94	−0.94	0.99	1.09	0.73	−0.84	1.25	1.02	0.30	−1.06
No positive feeling	1.44	0.95	−0.89	−0.89	1.10	1.08	0.50	−1.08	1.48	1.03	0.14	−1.13
Breathing difficulties	0.96	1.02	−0.80	−0.80	0.77	1.02	1.07	−0.16	1.01	0.95	0.59	−0.65
No initiative	1.24	1.04	−1.08	−1.08	1.41	1.10	0.20	−1.28	1.67	1.04	−0.19	−1.15
Overreact	1.17	0.92	−0.62	−0.62	1.22	1.06	0.43	−1.05	1.48	0.99	0.07	−1.03
Tremble	0.93	1.06	−0.71	−0.71	0.98	1.13	0.73	−0.94	1.03	0.95	0.58	−0.63
Nervous energy	1.54	0.91	−0.83	−0.83	1.45	1.07	0.13	−1.24	1.38	0.95	0.21	−0.87
Worried about panic	1.03	1.05	−0.90	−0.90	1.09	1.06	0.52	−1.01	1.16	0.97	0.45	−0.77
Nothing to look forward	1.47	1.07	−1.24	−1.24	1.31	1.15	0.31	−1.34	1.53	1.09	0.02	−1.30
Agitation	1.72	0.94	−0.82	−0.82	1.52	1.04	0.12	−1.18	1.71	0.88	−0.06	−0.83
Difficult to relax	1.69	.97	−1.01	−1.01	1.55	1.08	0.01	−1.30	1.73	1.03	−0.26	−1.11
Down-hearted	1.64	1.06	−1.22	−1.22	1.55	1.08	0.04	−1.30	1.70	1.10	−0.23	−1.29
Intolerant	1.14	0.93	−0.73	−0.73	1.07	1.03	0.56	−0.87	1.31	0.94	0.27	−0.81
Panic	0.93	1.07	−0.72	−0.72	1.09	1.13	0.51	−1.20	1.12	1.01	0.40	−1.01
Not enthusiastic	1.30	1.04	−1.09	−1.09	1.18	1.16	0.46	−1.27	1.47	1.07	0.04	−1.25
Worthlessness	1.45	1.08	−1.26	−1.26	1.13	1.16	0.50	−1.24	1.37	1.11	0.19	−1.30
Touchy	1.36	0.90	−0.72	−0.72	1.58	1.03	−0.01	−1.18	1.75	1.01	−0.19	−1.14
Heart-aware	1.14	1.02	−1.08	−1.08	1.11	1.13	0.57	−1.10	1.19	1.03	0.36	−1.05
Scared	0.96	0.98	−0.60	−0.60	1.05	1.09	0.63	−0.94	1.19	0.99	0.41	−0.88
Meaningless	1.21	1.10	−1.24	−1.24	1.08	1.15	0.55	−1.21	1.36	1.11	0.20	−1.33

Abbreviations: Ku, kurtosis; *SD*, standard deviation; Sk, skewness.

structure equality (Williams, 2021). The omnibus test was followed by the local check of edge differences based on the Bayes factor. This approach also allows estimating 99% credible intervals of posterior means (Williams, 2021), which is essential to clarify the practical significance of edge differences. To safeguard against Type I errors, we emphasized only those differences between the networks that were replicated between these two methods, and considered the effect size of differences and their practical significance.

4 | RESULTS

4.1 | Descriptive statistics

The Serbian sample had the highest average scores on all three DASS-21 subscales, whereas the Croatian sample had the lowest (Table S2). The differences on all three subscales were significant but only between the Serbian and Croatian samples (Dep: $F_{[2,\ 312.84]} = 5.7838$, $p = .003$, $\xi = .17$; Anx: $F_{[2,\ 307.12]} = 3.6493$, $p = .027$, $\xi = .13$; Str: $F_{[2,\ 312.09]} = 4.4239$, $p = .013$, $\xi = .15$).

The mean item score in the Italian sample was 1.28 ($SD = .24$); in the Croatian, it was 1.22 ($SD = .22$); and 1.40 ($SD = .23$) in the Serbian sample (Table 2). All items in all three samples were sufficiently informative (i.e., had sufficient variability) and were included in the analyses. Additionally, scalar (thresholds) invariance as well as loading and threshold invariance held for the three samples, supporting the notion that the items behave similarly within the three languages/cultures (Tables S3 and S4). Also, the reliability of the DASS-21 can be found in Table S5.

4.2 | Network estimation of the DASS-21 across the three samples

The network estimation is presented in Figure 1. Estimated networks were rather dense and fairly comparable regarding the number of non-zero edges and average edge weights (Italian: 140 non-zero edges out of 210 and .046; Croatian: 108 non-zero edges and .047; Serbian: 108 non-zero edges and .046).

In all three networks (Figures 2 and 3), *Down-hearted* was among the most central symptoms. In the Croatian and the Italian networks, *Agitation* seemed to be also central, but not in the Serbian network. *Nervous energy* was among the strongest nodes in the Croatian and Serbian networks, but not in the Italian. On the other hand, *Difficulty to relax* was one of the most central symptoms in the Serbian network, but not in the other two. *Breathing difficulties* was important only in the Italian network.

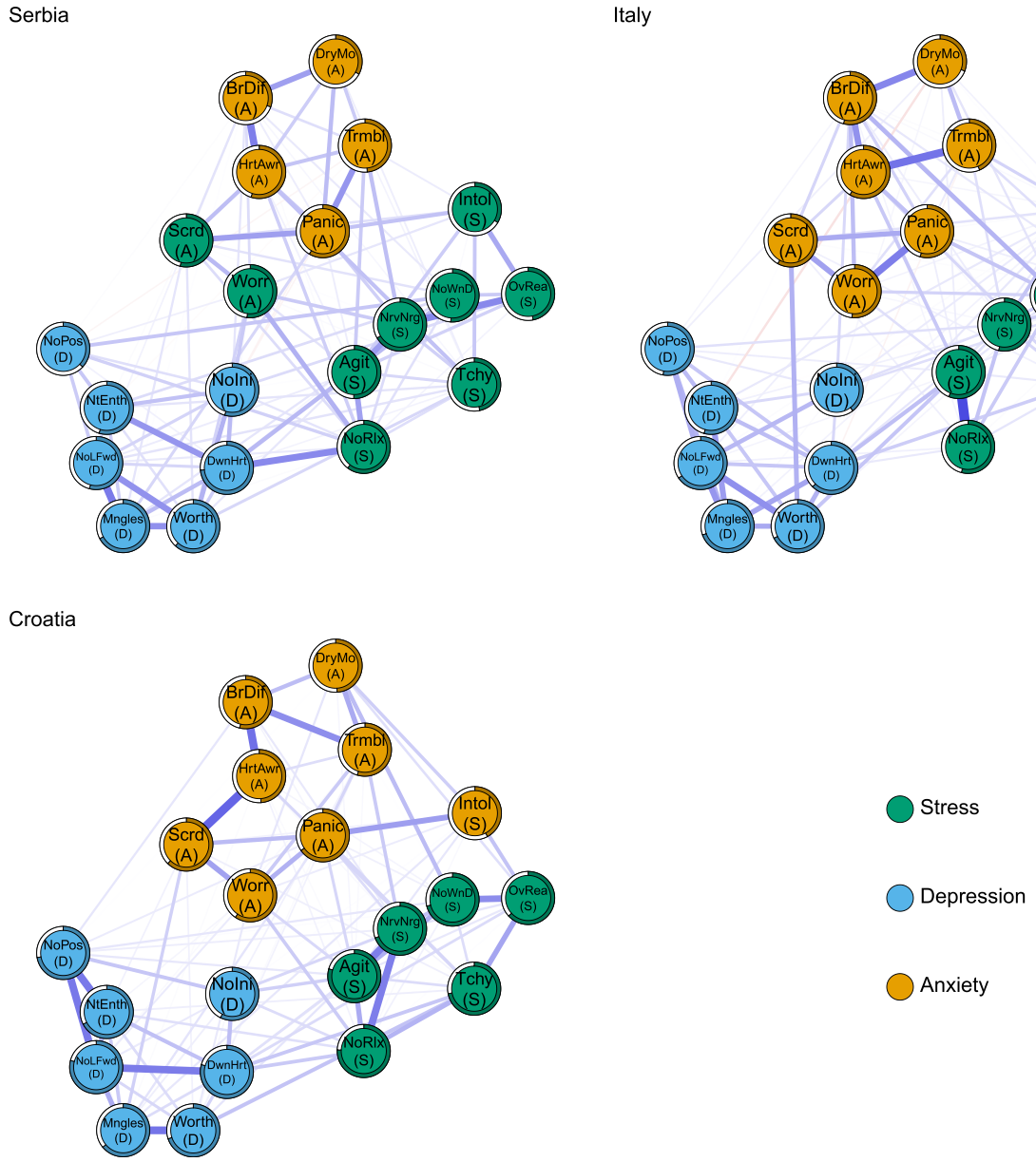

FIGURE 1 Regularized partial correlation networks of the DASS-21 with community analysis across three samples presented in an averaged layout. Thicker edges indicate stronger association (blue—positive; red—negative). The colored area of the ring around the nodes represents predictability (the variance of a node explained by all its neighbors). Different colors represent the membership of nodes into different communities (the walktrap algorithm used). Agit, agitation; BrDif, breathing difficulties; DryMo, dry mouth; DwnHrt, down-hearted; HrtAwr, heart-aware; Intol, intolerant; Mngles, meaningless; NoIni, no initiative; NoLFwd, nothing to look forward; NoPos, no positive feeling; NoRlx, difficult to relax; NoWnD, hard to wind down; NrvNrg, nervous energy; NtEnth, not enthusiastic; OvRea, over-react; panic, close to panic; Scrd, scared; Tchy, touchy; Trmbl, tremble; Worth, worthlessness; Worr, worried about panic.

To estimate the similarity of the strength centrality structure of the three networks, we computed the correlations between node strengths across the three samples (Borsboom et al., 2017). They were of moderate magnitude ($r_{cItalianCroatian} = .614$, $r_{cCroatianSerbian} = .522$ and $r_{cItalianSerbian} = .452$), indicating a medium level of similarity regarding the node centrality. It is important to note that the strength centrality of the nodes was not correlated with items' variability ($r_{Italian} = .31$, $p = .17$, $r_{Serbian} = .31$, $p = .17$, and $r_{Croatian} = .07$, $p = .77$). The average predictability in the three samples was somewhat similar across the three samples (Italian sample = .522; Croatian = .658; and Serbian = .528), suggesting that in all three samples, more than 50% of the node's variance was explained by the neighboring nodes.

The inspection of the differences in the node strengths (Figure 3) additionally supported the findings about similarities and differences among the networks. The largest number of significant differences between the nodes was present in the Italian sample, followed by the Croatian, and then the Serbian sample. In the Italian

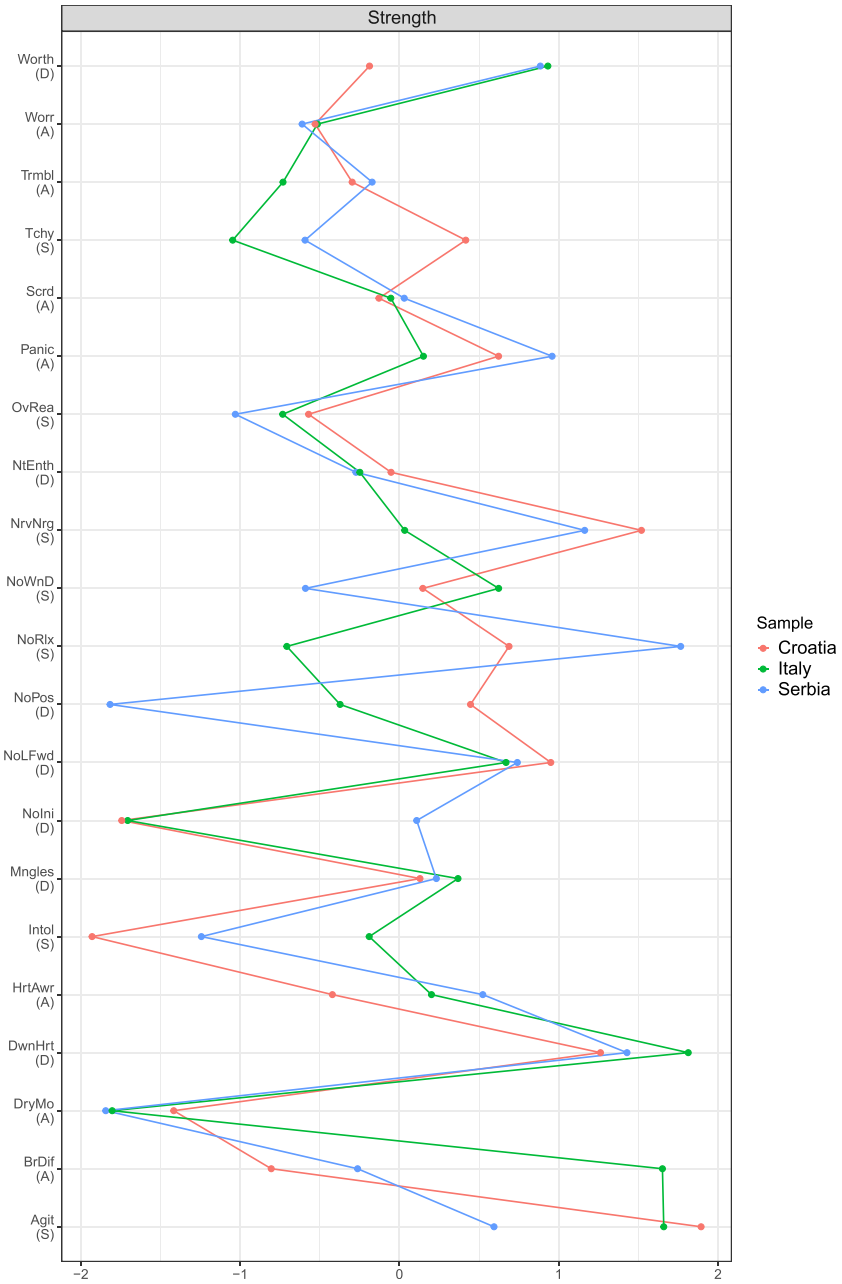

FIGURE 2 Comparative strength centrality of the DASS-21 in the three networks, shown as standardized scores.

sample, *Down-hearted*, *Agitation* and *Breathing difficulties* comprised the group of the strongest symptoms, and they were significantly stronger than 13, 11 and 12 other symptoms, respectively. In the Croatian sample, *Agitation* was the strongest node by far. It was significantly stronger than all the other symptoms except for the *Nervous energy*, *Down-hearted* and *Nothing to look forward*. In the Serbian sample, the strongest nodes were *Difficulty to relax* and *Down-hearted*. They were significantly stronger than 10 other symptoms.

4.3 | Network communities and bridges

The walktrap algorithm detected three communities in all samples. In the Serbian sample, the spinglass algorithm yielded three communities in 80% of 1000 random trials; in Italian, four communities in 53% (3 communities in 35%); and in the Croatian sample, three communities in 89% of trials. The optimal algorithm detected three communities in all three samples. We opted for the walktrap algorithm

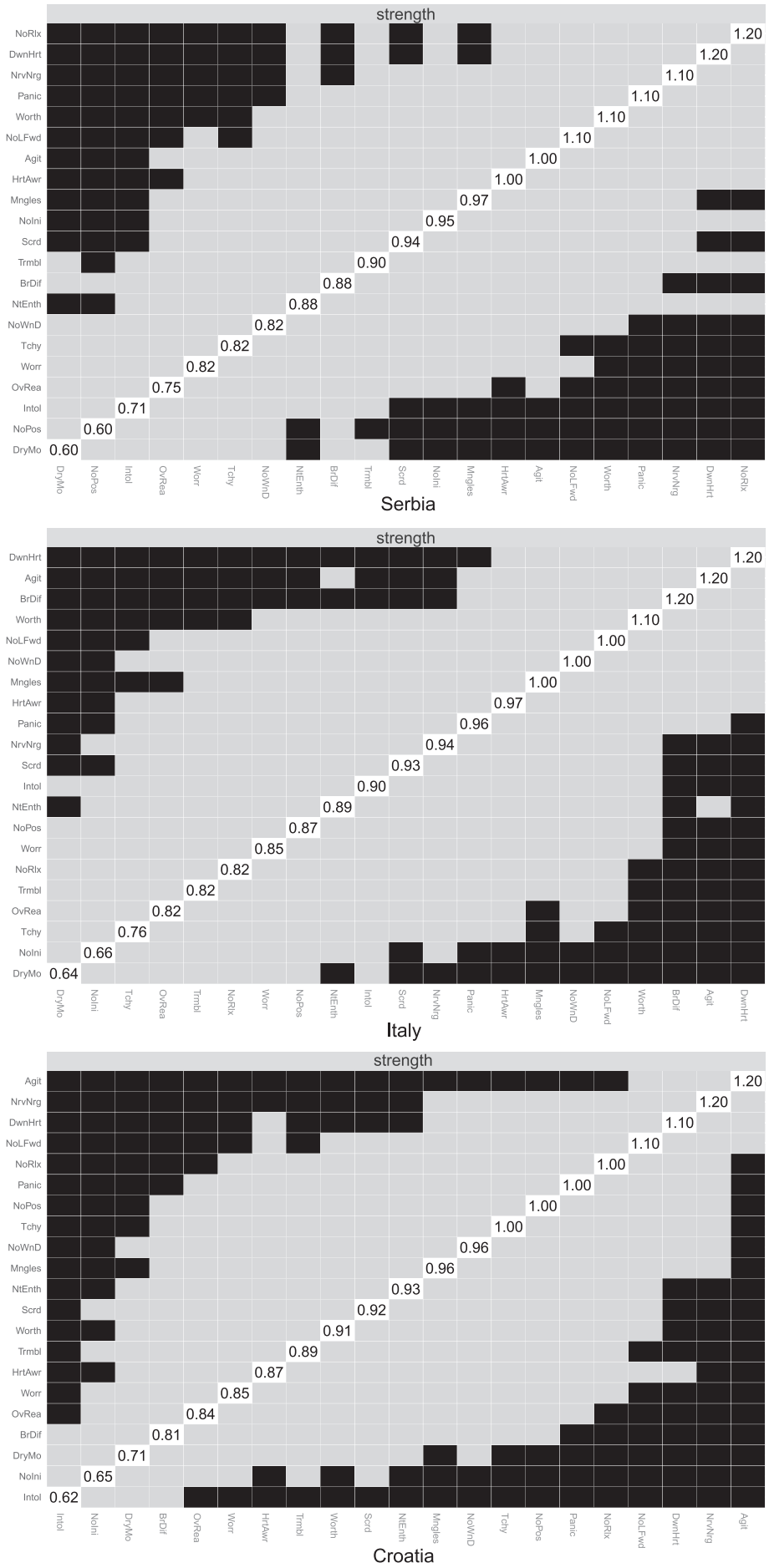

FIGURE 3 Nonparametric bootstrapped difference test for strength in the three networks.

because it provided the most interpretable solution in the three samples and in line with previous findings.[2]

In the Italian sample, the three communities were identical to the previous factor-analytics studies (Bottesi et al., 2015; Henry & Crawford, 2005), with seven items per community. In the Croatian sample, the only difference in comparison to the previous studies was that *Intolerant* was included in the anxious/autonomic arousal community. In the Serbian sample, two symptoms, namely, *Scared* and *Worried about panic*, from the anxious/autonomic arousal domain (Mihić et al., 2021) were included in the stress/stress community.

We also estimated bridges among the communities (Figure S3). Coefficients of the stability for the bridge strength were satisfactory for all three networks (Table S1), as well as their accuracy (Figure S4). In the Italian network, *Agitation* and *Hard to wind down*, both from the stress/tension community, had the highest bridge centrality. *Agitation* had relatively strong edges with *Down-hearted* and *Worthlessness* (depression community), and with *Heart awareness* (anxious/autonomic arousal). *Hard to wind down* had relatively strong edges with three symptoms from the anxious domain, namely, *Breathing difficulties*, *Panic* and *Worried about panic*. Within the Croatian sample, two symptoms from the stress/tension community, *Agitation* and *Touchy*, had the strongest bridge centrality. *Agitation* had relatively strong edges with *No initiative* from the depressive domain, and somewhat weaker with *Panic* and *Worried about panic* from the anxious/autonomic arousal domain. *Touchy* had relatively strong edges with *Worthlessness* and *Down-hearted* from the depressive domain. In the Serbian network, the strongest bridges were *Panic* (anxious/autonomic arousal) and *Inability to relax* (stress community). *Panic* had relatively strong connections with *Intolerant* and *Nervous energy* (both from the stress community). *Inability to relax* had relatively strong edges with *Down-hearted* (depression community) and *Worried about panic* and *Heart awareness* from the anxiety/autonomic arousal community.

4.4 | Network comparison across the three samples

The correlations between the weights of the same edges across the three networks suggested a moderate amount of similarity ($r_{IC} = .413$, $r_{CS} = .402$, $r_{IS} = .340$). The NCT test suggested no significant differences in the global network connectivity across the three samples (Table S6). The omnibus test of maximal difference was significant only for the Serbian and Italian networks (Table S6). Following this omnibus test, the permutations test between these two networks revealed 10 significant differences in edge weights, namely, *Hard to wind down–No enthusiastic*, *Hard to wind down–Touchy*, *Agitation–Difficult to relax*, *No positive feeling–Meaningless*, *No Initiative–Worthlessness*, *Tremble–Close to panic*, *Tremble–Heart-aware*, *Nervous energy–Intolerant*, *Worried about panic–Down-hearted* and *Worried about panic–Close to panic*. Since the Italian network had 114 non-zero edges, while the Croatian and the Serbian networks had 108 each, this number of the significantly different edge weights can be considered rather small. However, we must note that edge weights accuracy analysis revealed wide 95% confidence intervals, which may result in a smaller number of significant differences (Figure S5).

The Bayesian omnibus test based on posterior predictive check found that the three network structures were different (Jenson–Shannon divergence $JSD_{Serbia-Italy} = 2.133$, $JSD_{Serbia-Croatia} = 1.937$ and $JSD_{Serbia-Italy} = 2.099$, all $p = .001$). Local Bayes factor testing showed moderate support (BF > 3) for the difference between 18 edges in the Serbian and Italian networks, 15 edges in the Serbian and Croatian networks and 13 edges in the Italian and Croatian networks (see Table S7). To assess the practical meaningfulness of these differences we used 99% credible intervals of posterior means (Figure S6). The analysis revealed that there were only three differences between the Serbian and the Italian networks, two between the Serbian and the Croatian networks and three between the Italian and the Croatian networks that could be considered non-trivial (Table S7) and of moderate effect size (Cohen, 1988). Overall, the difference between the *Worried about panic–Panic* edges in the Serbian and the Italian samples was the only difference detected as non-zero by both the NCT and Bayesian approaches, suggesting that this edge was stronger in the Italian sample. Given that the three samples differed according to their diagnostic composition, a moderated network analysis was conducted and suggested that the diagnostic status did not influence our results (Table S8 and Figure S7).

5 | DISCUSSION

We found a moderate degree of similarity across the three networks regarding centrality. The *Down-hearted* was among the most central symptoms within each network. Specific stress symptoms within each network, such as *Agitation*, *Nervous energy* and *Difficulty to relax*, also played a central role and did not differ from *Down-hearted* in their centrality. Only within the Italian network, some anxiety/autonomic arousal symptoms (panic/difficulty breathing) were of equal strength as these depression and stress symptoms. Our findings support the notion that depression, stress/tension and anxiety/autonomic arousal are parts of the same broad network, rather than separate diagnostic entities (Boschloo et al., 2015; Fried et al., 2016; Van den Bergh et al., 2021). The observed variations among the three networks in centrality may reflect several influences. In fact, many cross-cultural factors can modulate the expression of depression, anxiety and other disorders, such as religion (Braam et al., 2001), social welfare (Everson et al., 2002), understanding of self and body (Halbreich et al., 2007), different diagnostic practices across the countries (Ahmed &

[2]Different algorithms gave quite similar solutions (i.e., walktrap and spinglass), but the detected communities were never completely identical (with the exception of the Croatian sample). Walktrap and optimal algorithms identified identical communities in the Italian sample, but when using the spinglass algorithm, *Difficulty to relax* and *Agitation* formed a separate community, apart from other stress-related symptoms. In the Serbian sample, when using spinglass and optimal algorithms, *Hard to wind down* shifted to the community of depressive symptoms, but *Scared* joined the other symptoms of anxiety. Overall, the differences were small, and the symptoms that shifted between two communities had comparable connections with both them.

Bhugra, 2006) and even underlying genetic factors (Chiao & Blizinsky, 2010). These factors can indeed influence the way people experience and complain about symptoms, although methodological differences may also play a role (Van de Vijver & Leung, 1997).

Our findings revealed that within the Italian, Serbian and Croatian networks, the symptoms clustered in three communities. The Italian network was completely in line with the previous factor-analytic work revealing seven items per community (Bottesi et al., 2015). Within the Croatian and Serbian networks, one and two items, respectively, were positioned differently than what would be expected based on the previous factor-analytic studies carried out in these two cultures (Ivezic et al., 2012; Mihić et al., 2021). In the Croatian sample, item *Intolerant* had the highest edge with *Panic*, which probably led to its inclusion within the anxiety/anxious arousal community. In the Serbian sample, *Worried about panic* and *Scared* were more tightly linked with the stress/tension community than with the anxiety/autonomic arousal community. Even though *Scared* had the highest edge with *Panic*, it also had weaker connections with the number of stress/tension symptoms, which probably led to its placement within this community. In a different Serbian study using bifactor modeling, these two items also did not load on the anxiety factor (Mihić et al., 2021). Hence, in the Serbian network, it seems that fear reactions and the symptoms of tension are more intertwined than in the Croatian and Italian networks. Given a lack of research on differences in the expression of distress in these three countries, these interpretations should be regarded as tentative.

We also identified bridge symptoms and examined them while considering all three communities at once. Although the combination of the symptoms that had the highest bridge centrality differed across the three networks, in each network the stress/tension symptoms (*Agitation*, *Touchy*, *Inability to relax* and *Hard to wind down*) acted as the bridges, with the inclusion of *Panic* (anxiety community) in the Serbian network. These stress/tension symptoms were tightly connected with the symptoms from both the depression and anxiety/autonomic arousal communities, suggesting that they might be good targets for intervention.

The stress symptoms (*Being restless* and *Inability to relax*) were reported to be important bridges to the depression community in other studies on clinical samples (Beard et al., 2016; Kaiser et al., 2021). Since the publication of the DSM-5 (2013), it has been recognized that anxious distress might characterize many patients diagnosed with major depressive disorder. For example, the prevalence of this type of depression seems to range between 40% and 78% (Thase et al., 2017). Also, agitation seems to be present during depression episodes in 32.2% of bipolar patients (Serra et al., 2019). Moreover, anxious depression is associated with poorer functioning, limited response to treatment and greater suicidality (Thase et al., 2017). It has also been noted that depression tends to be episodic, while anxious symptoms tend to linger and hardly remit completely (Thase et al., 2017). Finally, some studies suggested that in 57% of cases, anxiety disorders preceded comorbid depressive disorders, whereas in only 18% of cases, depression disorder preceded anxiety disorders (Lamers et al., 2011). Hence, it may be important to clinically target the stress/tension symptoms in order to prevent exacerbation of the symptoms and depression recurrence.

Similar stress symptoms acted as bridges toward the anxiety/autonomic arousal community in all three networks in the current study. This level of similarity is striking given that our participants came from different countries and had various clinical diagnostic profiles. For example, in both the Italian and Croatian networks, *Agitation* seemed to be most closely linked with *Heart awareness* (Italian network), and *Panic* and *Worried about panic* (Croatian network). In the Italian network, one additional stress symptom (*Hard to wind down*) was connected significantly with the anxiety/autonomic arousal network, in particular with the symptoms of *Breathing difficulties*, *Panic* and *Worried about panic*. In the Serbian network, *Inability to relax* seemed to be a bridge towards the symptoms of *Worried about panic* and *Heart awareness* both from the anxiety/autonomic arousal network. Additionally, in this network, *Panic* had the highest bridge centrality and had close connections with the stress symptoms of *Intolerant* and *Nervous energy*.

Different authors have recognized the close links between stress/tension and panic/autonomic arousal. For example, increased tension can be an internal triggering stimulus that, via catastrophic misinterpretations, can lead to a full-blown panic attack in individuals with panic disorders (Clark, 1986). Also, the initial level of tension, prior to exposure to panicogenic agents such as CO_2, heightens the probability of the development of a panic attack during an experiment in persons with panic disorders (Barlow, 2002). Others have also noted that panic and anxiety are distinct but functionally related states (McNaughthon & Corr, 2008), with some even suggesting that both agitated (anxious) depression and panic might have similar biological mechanisms, such as increased catecholamine levels (Serra et al., 2019).

We also analyzed differences in edge weights within and across the three networks. There were moderate correlations between the same edges across the three networks. Two separate analyses converged on suggesting that only one edge (*Worried about panic–Panic*) differed between the Serbian and the Italian networks. This edge was non-existent within the former and was one of the strongest within the latter. A moderated network analysis using the participants' diagnostic status as a moderator did not suggest that the *Worry about panic–Panic* difference between these networks could be attributed to concurrent psychopathology (see Table S8 and Figure S5). A reason for this difference may be methodological rather than substantial. In fact, in the official Serbian translation,[3] the term 'worried' was translated to denote actual fear response to panic-related situations rather than the anticipatory worry process regarding potential panic situations, as intended in the original item. This explanation is in agreement with a recent commentary outlining that many translations that can be found on the official DASS Website do not necessarily represent actual adaptations that take into account language and culture during the translation process (Carlson, 2020).

[3](http://www2.psy.unsw.edu.au/dass/serbian/serbian.htm).

In sum, it is worth stressing that the network structure of depressive, anxiety and stress symptoms was markedly stable in psychiatric samples, across different languages and countries (e.g., Italy, Serbia and Croatia). Even though the three countries differ in the level of individualism, such differences might not have been sufficient to lead to substantial divergences in the depression–anxiety networks in this study. The specific differences that our analysis revealed might be rather consequences of linguistic and translation peculiarities than more global cultural characteristics.

5.1 | Strengths and limitations

This study has several limitations. First, its cross-sectional nature precluded the detection of directionality in our networks. Future studies should evaluate the temporal dynamics of depression, anxiety and stress by incorporating time into the study design. Second, symptoms were measured only with self-report questionnaires. Although this approach did not allow us to disentangle subjective complaints from clinical symptoms, the DASS-21 represents one of the most validated and internationally used questionnaires for measuring these three phenomena. Third, our psychiatric samples included several psychiatric disorders, which were not fully balanced among the three networks; therefore, future studies should aim at recruiting diagnostically homogeneous samples across different countries. Finally, similar to other network studies that had a cross-cultural focus (de la Torre-Luque et al., 2020; Fonseca-Pedrero et al., 2018; Fried et al., 2018), this study was largely exploratory limiting the degree to which we can theorize about the way culture shapes the expression of distress. However, our samples represent naturalistic samples, as encountered by professionals in the respective countries, and this appears a point of strength of the current study. Interestingly, more than half of the Italian sample consisted of patients with externalizing psychopathologies, while the Serbian and Croatian samples mainly included people with internalizing psychopathologies. Thus, the similarities that emerged across the three samples may suggest that current results may be relevant also from a transdiagnostic perspective.

6 | CONCLUSION

In conclusion, we believe that our study represents a valuable contribution to the investigation of the comorbidity phenomenon from a cross-cultural point of view. We showed that the network structure and features in mixed clinical samples are similar across three different languages and cultures. The probability that our findings are due to chance fluctuations is slim given the following: (i) networks regularization procedure used to ensure only existing edges were modeled, (ii) bootstrapping of edges and centrality indices (to assess the accuracy of the edges and stability of the centrality indices), (iii) testing of networks' differences using multiple procedures (NCT and Bayesian approaches) and (iv) focusing only on differences having at least moderate effect size. Moreover, our research revealed that, while negative mood emerged to be the most central node, stress nodes were the most likely bridge symptoms between depressive and anxiety symptoms. Hence, future studies should investigate whether these elements of the network may represent important loci of clinical intervention. Future studies may also want to further broaden the focus, by comparing socio-culturally and geographically more distant countries.

CONFLICT OF INTEREST STATEMENT

No conflict of interest.

DATA AVAILABILITY STATEMENT

The Spearman's variance–covariance matrices for the Italian, Serbian, and Croatian data can be found online (https://osf.io/wjnr9/).

ETHICS STATEMENT

Serbia: Ethical committee of the Faculty of Philosophy, University of Novi Sad, Serbia, and the Ethical boards of the institutions that provided patients. Croatia: Ethical Committees of the two psychiatric institutions. Italy: Ethics Committee for Psychological Research of the University of Florence, Florence, Italy and Ethics Committee for Psychological Research of the University of Padova, Italy.

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