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A network analysis of DSM-5 posttraumatic stress disorder symptoms and correlates in U.S. military veterans

Cherie Armour[a,*,1], Eiko I. Fried[b,1], Marie K. Deserno[c], Jack Tsai[d,e], Robert H. Pietrzak[d,f]

[a] Psychology Research Institute, Coleraine Campus, University of Ulster, Coleraine, Northern Ireland, BT52 1SA, UK
[b] Faculty of Psychology and Educational Sciences, University of Leuven, Leuven, Belgium
[c] Department of Psychology, University of Amsterdam, Amsterdam, The Netherlands
[d] Department of Psychiatry, Yale University School of Medicine, New Haven, CT, USA
[e] United States Department of Veterans Affairs, New England Mental Illness Research, Education, and Clinical Center, West Haven, CT, USA
[f] United States Department of Veterans Affairs, National Center for Posttraumatic Stress Disorder, Clinical Neurosciences Division, West Haven, CT, USA

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ABSTRACT

Objective: Recent developments in psychometrics enable the application of network models to analyze psychological disorders, such as PTSD. Instead of understanding symptoms as indicators of an underlying common cause, this approach suggests symptoms co-occur in syndromes due to causal interactions. The current study has two goals: (1) examine the network structure among the 20 DSM-5 PTSD symptoms, and (2) incorporate clinically relevant variables to the network to investigate whether PTSD symptoms exhibit differential relationships with suicidal ideation, depression, anxiety, physical functioning/quality of life (QoL), mental functioning/QoL, age, and sex.
Method: We utilized a nationally representative U.S. military veteran's sample; and analyzed the data from a subsample of 221 veterans who reported clinically significant DSM-5 PTSD symptoms. Networks were estimated using state-of-the-art regularized partial correlation models. Data and code are published along with the paper.
Results: The 20-item DSM-5 PTSD network revealed that symptoms were positively connected within the network. Especially strong connections emerged between nightmares and flashbacks; blame of self or others and negative trauma-related emotions, detachment and restricted affect; and hypervigilance and exaggerated startle response. The most central symptoms were negative trauma-related emotions, flashbacks, detachment, and physiological cue reactivity. Incorporation of clinically relevant covariates into the network revealed paths between self-destructive behavior and suicidal ideation; concentration difficulties and anxiety, depression, and mental QoL; and depression and restricted affect.
Conclusion: These results demonstrate the utility of a network approach in modeling the structure of DSM-5 PTSD symptoms, and suggest differential associations between specific DSM-5 PTSD symptoms and clinical outcomes in trauma survivors. Implications of these results for informing the assessment and treatment of this disorder, are discussed.

1. Introduction

The nosology of posttraumatic stress disorder (PTSD) is highly controversial and widely debated (Hoge et al., 2016; Friedman, Kilpatrick, Schnurr, & Weathers, 2016). There have also been several changes to the diagnostic criteria since the initial introduction of PTSD into the *Diagnostic and Statistical Manual of Mental Disorders* (DSM). These changes include the definition of the criterion A trauma, the number and nature of symptoms (DSM-5 now includes three new diagnostic symptoms of negative belief, distorted blame, and recklessness), the number and nature of symptom groups, and the recent inclusion of a dissociative PTSD subtype. The latest version of the criteria (DSM-5) was released in May 2013. The current study utilizes a novel psychometric approach based on *Network Analysis* to identify the way in which DSM-5 PTSD symptoms interact at the individual item level and in turn to identify if these interactions are clinically relevant.

PTSD is an impairing disorder that affects a significant proportion of both civilians and military personnel exposed to a traumatic

* Corresponding author.
E-mail address: armour.cherie@gmail.com (C. Armour).
[1] These authors share first authorship.

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event (Karam et al., 2014; Kessler et al., 2014; Pietrzak, Goldstein, Southwick, & Grant, 2011). The estimated prevalence rates in military veteran populations range from 9 to 30% (Lapierre, Schwegler, & Labauve, 2007; Sundin, Fear, Iversen, Rona, & Wessely, 2010; Tsai et al., 2014). Veterans displaying posttraumatic symptomatology have greater difficulty with re-integration to civilian life post-deployment (Karstoft, Armour, Andersen, Bertelsen, & Madsen, 2015); report a lower quality of life (QoL) (Giacco, Matanov, & Priebe, 2013); and have greater risk for suicidal ideation (SI) (Jakupcak, Cook, Imel, Rosenheck & McFall, 2009; Jakupcak et al., 2011). PTSD is additionally a highly comorbid disorder with the vast majority of individuals also meeting the criteria for at least one additional psychiatric disorder (Brady, Killeen, Brewerton, & Lucerini, 2000; Pietrzak et al., 2011).

1.1. PTSD as characterized by the DSM-5

The most recent edition of the DSM (DSM-5; APA, 2013) characterizes PTSD as containing 20 individual symptoms that are grouped across four symptom clusters; Intrusions (IN; B1-B5; see Fig. 1), Avoidance (AV; C1-C2), Negative alterations in cognitions and mood (NACM; D1-D7), and Alterations in arousal and reactivity (AAR; E1-E6). Of note, the structure of PTSD in the DSM-5 has been contended with alternative structural models being proposed. In summary, a number of factor analytic studies have demonstrated that models comprising six (Liu et al., 2014 [Anhedonia Model]; Tsai et al., 2014 [Externalizing Behaviors model]) and seven symptom groupings (Armour et al., 2015 [Hybrid model]) may provide better fit than the four clusters outlined in the DSM-5 (reviewed in Armour, Mullerova, & Elhai, 2016).

A diagnosis of PTSD as set by DSM-5 criteria currently requires that trauma survivors endorse a minimum of six symptoms (at least 1 IN, 1 AV, 2 NACM, and 2 AAR), in addition to reporting significant functional impairment and the persistence of symptoms in excess of one month (APA, 2013). Notably, this prescribed six-item diagnostic algorithm has previously been reported as being so amorphous in nature that it results in 636,120 combinations of PTSD symptomatology (Galatzer-Levy & Bryant, 2013). Consequently, it is possible that individuals with a DSM-5 PTSD diagnosis can have remarkably distinct symptom presentations. Another potential drawback of the current criteria is that individuals who fail to meet them (by exhibiting less than six symptoms in the prescribed DSM-5 fashion) may be as impaired by their symptomatology as individuals who do meet the criteria. For example, failing to endorse at least one avoidance item would preclude someone from the diagnosis even if all other items in all other symptom groups were endorsed.

1.2. PTSD as a categorical or dimensional disorder

Although the DSM acknowledges that psychiatric disorders are dimensional, its guidelines maintain that a threshold on the dimension is required in order to define who does vs. does not receive a diagnosis; the DSM-5 nosology for PTSD is thus embedded, from a diagnostic point of view, in a categorical framework. Contrasting this categorical approach, many researchers support a dimensional view to PTSD, stating that the distress experienced by an individual post-trauma exists on a continuum in which the high end reflects more severe distress (cf. Ruscio, Ruscio, & Keane, 2002). In this case, symptoms that reflect PTSD are summed together to determine the position of an individual on the continuum. These sum scores are often used by researchers to assess the PTSD construct, particularly as it relates to the longitudinal course of symptoms (Bonanno, Papa, Lalande, Westphal, & Coifman, 2004; Dickstein, Suvak, & Litz, 2010; Karstoft, Armour, Elklit, & Solomon, 2013) and in assessing PTSD treatment response over time (Richardson et al., 2014).

1.3. A network approach to PTSD

Irrespective of whether the syndrome of PTSD is viewed through a categorical or dimensional lens – which is also not the focus of the current paper – the commonality between these view-

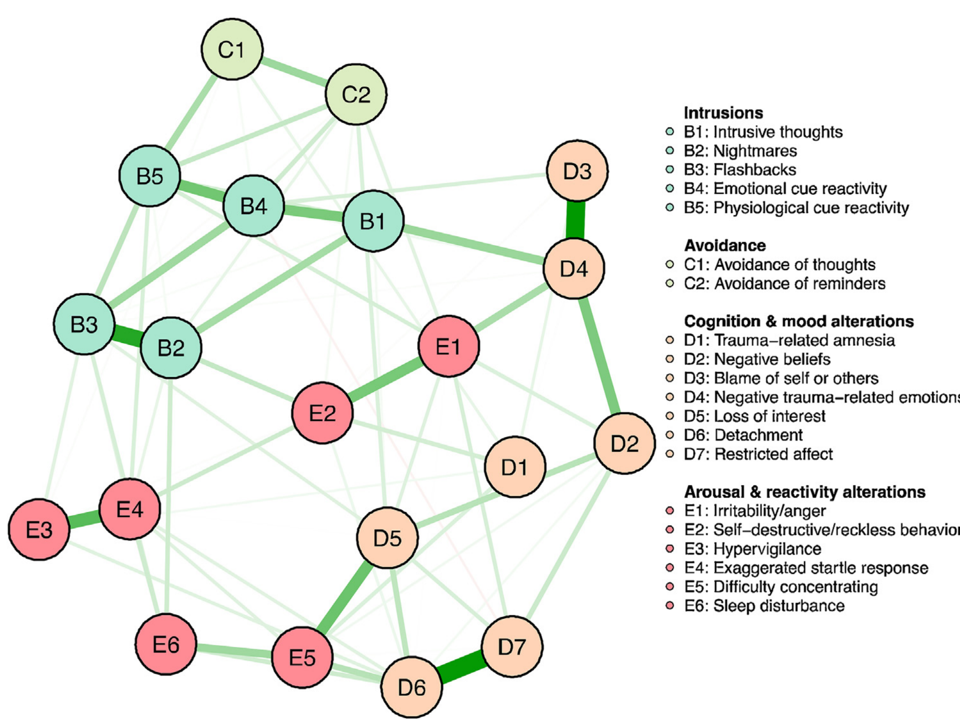

Fig. 1. Network containing the 20 DSM-5 symptoms of PTSD. Green lines represent positive associations, red lines negative ones, and the thickness and brightness of an edge indicate the association strength. For a color version of this Figure, we refer the reader to the online version of this paper. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

points is the proposition that symptoms are reflective indicators of an underlying latent construct that is PTSD. This 'reflective model' is the prevailing perspective with which psychopathology is currently viewed and understood (Borsboom & Cramer, 2013; Borsboom, 2008; Cramer, Waldorp, van der Maas, & Borsboom, 2010). In both categorical and dimensional systems, PTSD symptoms are interchangeable and equally reflective of the latent construct that is PTSD; this view is known as the 'common cause hypothesis' (Fried, 2015; Schmittmann et al., 2013). A challenge is that symptom groupings as outlined in the DSM (detailed above) have been shown to vary in relation to the precipitating traumatic event (Armour & Shevlin, 2010); vary in their comorbidity with alternative disorders (Contractor et al., 2014; Pietrzak, Tsai, Armour, Mota, Harpaz-Rotem, & Southwick, 2015; Roley et al., in press); relate differentially to perceived quality of life (Giacco et al., 2013); and display differential responses to treatment (Asmundson, Stapeleton, & Taylor, 2004). This implies that PTSD symptoms are not (roughly) interchangeable indicators of one underlying reflective latent variable that causes the covariation among symptoms. In addition, cross-sectional studies have revealed that different groups of individuals, displaying different symptom profiles, show differential associations with external variables (Ayer et al., 2011; Au, Dickstein, Comer, Salters-Pedneault, & Litz, 2013; Breslau, Reboussin, Anthony, & Storr, 2005; Alman et al., 2012; Maguen et al., 2013; Naifeh, Richardson, Del Ben, & Elhai, 2010; Rosellini, Coffey, Tracy, & Galea, 2014).

That symptoms do not interact with each other causally is highly implausible, as psychiatric symptoms by their very nature have direct relations to one another. McNally et al. (2015) exemplified this for PTSD, showing that being presented with a reminder of a traumatic event may in turn trigger psychological and physiological reactions, which may activate avoidance behaviors. This has important clinical implications, given that the ability to identify particular central symptoms in a causal system (symptoms that are highly connected and likely to trigger other symptoms), would allow clinicians to focus on such symptoms in assessment, monitoring, and treatment (Cramer et al., 2013; Fried, Epskamp, Nesse, Tuerlinckx, & Borsboom, 2015). From the traditional perspective of reflective latent variables that cause the covariance among symptoms, such specific symptom-focused interventions would generally not be employed.

A new and growing school of thought in which symptoms are related amongst themselves, rather than being equally reflective of an underlying latent construct, has been empirically tested by the development and application of data analytic techniques known as 'network analysis' (Borsboom & Cramer, 2013; Boschloo et al., 2015). From this perspective, symptoms are not *reflective* of an underlying disorder; instead, the associations among symptoms *constitute* the disorder. Networks are comprised of nodes (e.g., symptoms) and edges (associations among symptoms). Importantly, a network perspective does not assume symptoms to be interchangeable, but instead allows for the examination of the importance or centrality of symptoms empirically. Highly connected items that are likely to spread activation through the symptom network once activated are more central, whereas items with fewer connections lie on the periphery of a network and are less important (Borsboom & Cramer, 2013; Fried et al., 2015). The network approach to psychopathology has received growing attention and recognition in the last years, and a new review paper discusses its application to a wide variety of disorders, including major depression, psychosis, and autism (Fried et al., under revision).

To date, only a few studies have employed a network analysis of PTSD symptoms (Knefel Tran, & Lueger-Schuster, 2016; Afzalia et al., 2016; McNally et al., 2015). Both Knefel et al. (2016) and Afzalia et al. (2016) examined the way in which PTSD symptomatology associates with symptomatology of other disorders; the former assessed borderline personality disorder and the latter depression. McNally et al. (2015) focused solely on PTSD symptomatology (as we did in the current study) in 362 survivors of the Wenchuan earthquake in China. Key findings included: the centrality of the hypervigilance symptom; connections between anger, sleep, irritability, and concentration difficulties; and associations among intrusive thoughts, dreams, and flashbacks. The study analyzed the DSM-IV PTSD symptoms. In the current study, we estimated networks of PTSD symptoms using data from the National Health and Resilience in Veterans Study (NHRVS), which is a contemporary, nationally representative study of U.S military veterans. We extended the McNally et al. (2015) study in four ways: (1) for the first time, we constructed PTSD networks based on the DSM-5 rather than the DSM-IV criterion symptoms; (2) we employed a sub-sample of veterans reporting clinically significant PTSD symptoms from a representative U.S. veteran study; pertinent given the plethora of research detailing generally higher rates of symptomatology and comorbidity in this population (Giacco et al., 2013; Jakupcak et al., 2011; Karstoft et al., 2014; Tsai et al., 2014); (3) we estimated the network structure among PTSD symptoms, and also, for the first time, added a number of clinical covariates (SI, depression, anxiety, physical functioning/QoL, mental functioning/QoL, age, and gender) into the network to examine whether they display particular associations with particular PTSD symptoms; and (4) we analyzed the robustness and stability of the networks.

2. Methods

2.1. Sample

2.1.1. Participants

A total of 1484 (mean age = 60.4 years, SD = 15.3, range = 20–94) veterans aged 21 years and older participated in the second baseline cohort of the National Health and Resilience in Veterans Study (NHRVS), conducted from September–October 2013. The sample was collected using KnowledgePanel, a nationally representative survey research panel of more than 50,000 adults that represents approximately 98% of all U.S. households. KnowledgePanel is maintained by GfK, a survey research company based in Menlo Park, California, that uses probability-based sampling of addresses from the U.S. Postal Service's Delivery Sequence File (DSF) in its participant recruitment, including households both with and without telephone numbers and/or Internet access. Veterans completed a 60-min web-based survey that assessed a range of sociodemographic, psychiatric, and health variables. A total of 221 veterans met inclusion criteria (described below in detail) and were analyzed in this study. The data and analytic code are published in the Supplementary materials of this paper.

2.1.2. Assessments

2.1.2.1. Trauma exposure and PTSD symptoms. Veterans were administered the Trauma History Screen (THS; Carlson, Smith & Palmieri, 2011), which asked whether they had been exposed to any of 14 potentially traumatic events in their lifetimes. Veterans who endorsed multiple trauma exposures were asked, "Which of these experiences was the worst for you?". The Posttraumatic Stress Disorder Checklist for DSM–5 (PCL-5; Weathers, Blake et al., 2013; Weathers, Litz et al., 2013) was used to assess past-month symptoms of PTSD in relation to this worst event. The PCL-5 consists of 20 items (total score range: 0–80) that inquire about the extent to which an individual is bothered by each of the DSM-5 PTSD symptoms on a 5-point Likert scale: 0 = Not at all; 1 = A little bit; 2 = Moderately; 3 = Quite a bit; 4 = Extremely. Cronbach's alpha on PCL-5 items in the current sample was excellent (0.90).

2.1.2.2. Depression and anxiety symptoms. Current depression and anxiety symptoms were assessed using the Patient Health Questionnaire-4 (PHQ-4; Kroenke, Spitzer, Williams, & Löwe, 2009), a 4-item self-report screening instrument for depression and anxiety. Each construct is measured by two items. These items are summed and scores $\geq$3 on the depression and anxiety items are indicative of positive screens for depression and anxiety.

2.1.2.3. Suicidal ideation. SI in the past two weeks was assessed using two questions, adapted from the SI question in the Patient Health Questionnaire-9 (PHQ-9; Kroenke, Spitzer, & Williams, 2002), to assess both passive and active SI (Thompson, Henkel, & Coyne, 2004). Specifically, respondents were asked: "How often have you been bothered by thoughts you might be better off dead?" (passive SI) and "How often have you been bothered by thoughts of hurting yourself in some way?" (active SI). Since the current study already has a comparably large number of nodes compared to the number of participants, and because the correlation between active and passive SI was high (0.73), we only included active SI, which was coded as a response $\geq$1 (Several days).

2.1.2.4. Mental and physical functioning/QoL. The Short Form-8 Health Survey (SF-8; QualityMetric, 2014) measures QoL, functional health and well-being. It is a validated, abbreviated version of the SF-12 Health Survey (Ware, Kosinski, Turner-Bowker, & Gandek, 2002) and one of the most widely used measures of physical and mental functioning/QoL. Component mental and physical health summary scores range from 0 to 100, with a score of 50 representing the average level of functioning in the general population with each 10-point interval representing one standard deviation. Higher scores reflect better functioning.

2.2. Missing data and sample derivation

PCL-5 responses were used to identify veterans with clinically significant PTSD symptoms according to the following criteria: 1) probable past-month DSM-5 PTSD, defined by a total score of >38 on the PCL-5 (Hoge, Riviere, Wilk, Herrell, & Weathers, 2014); or 2) probable subthreshold PTSD, defined as endorsement of 2 or 3 B-E criteria, or endorsement of all 4 criteria but with total PCL-5 scores of under 38 (McLaughlin et al., 2014). Item-level data were missing for 1.6% of the sample and were imputed using an iterative Markov chain Monte Carlo (MCMC) method. A total of 221 veterans met either of the above criteria: 59 (weighted 27.7%) for probable past-month DSM-5 PTSD and 162 (weighted 72.3%) for probable subthreshold DSM-5 PTSD. Data from these 221 veterans were analyzed in this study.

2.3. Data analysis

Data and analytic code for this manuscript are available in the Online Supplementary materials.

2.3.1. Network estimation

We estimated the structure of three networks using the *R*-package *qgraph*. In a first step, we included the 20 PTSD symptoms in the estimation procedure (N1). Second, we added seven clinical covariates to the network that are outlined in detail above (N2): SI, depression, anxiety, physical QoL, mental QoL, age, and gender. In general, networks feature nodes (in our case: symptoms and clinical covariates) and edges (the connections among nodes). A main advantage of the network approach is that it visualizes the multivariate dependencies of the data that otherwise remain hidden. The most informative visualization, which we also choose here, is one in which edges can be understood as partial correlation coefficients, meaning that a connection between nodes A and B is the connection after controlling for all other edges in the network. To do so, we estimated a Gaussian Graphical Model that estimates pairwise association parameters between all nodes. With 20 symptom nodes, 190 pairwise association parameters are estimated, and 351 pairwise association parameters for the second network with 27 nodes. The estimation of that many parameters likely leads to a number of false positive connections, and we control for these by using the least absolute shrinkage and selection operator (LASSO) (Tibshirani, 1996) that sets very small edges to zero. In other words, the LASSO procedure employs a regularization technique that conservatively identifies only the relevant edges, and accurately discovers the underlying network structure (van Borkulo et al., 2014). More details on the estimation of such regularized partial correlation networks, including a tutorial that explains how to estimate such models in R, is available elsewhere (Epskamp & Fried, 2016). Since PTSD symptoms can be considered ordered-categorical, the estimation of the 20-item network is based on the polychoric correlation among symptoms. For the 27-item network that includes covariates, we used the cor_auto function of the *qgraph* package that automatically computes the appropriate correlations for different variable types (polychoric, polyserial, or Pearson).

In a last step, we examined the impact of covariates on the associations *among* the 20 PTSD symptoms. To do so, we deleted the 7 covariates from the adjacency matrix of the full 27-node network, which results in the connections among the 20 PTSD symptoms *controlling* for the 7 covariates (N2*). We subtracted this modified adjacency matrix N2* from the adjacency matrix of N1 (the 20 PTSD symptoms, not controlling for covariates) to derive a delta network (N3) that contains the *change* of N1 upon including the covariates.

2.3.2. Centrality estimation

For the 20-item PTSD symptom network, we were interested which symptoms are most relevant. There are three common graph theoretical centrality measures (Opsahl, Agneessens, & Skvoretz, 2010). (1) Node strength sums all edges of a given symptom with all other symptoms, estimating how strongly a node is directly connected with the network. (2) Closeness centrality provides a measure of how strongly a node is connected indirectly with the network by taking the inverse of all shortest path lengths between a node and all other nodes. (3) Betweenness centrality relies on the concept of shortest path length connecting any two symptoms, and a symptom with a high betweenness centrality can be considered to be central in connecting other symptoms.

2.3.3. Accuracy and stability estimation

When estimating psychopathological networks, a major current challenge is that the stability and accuracy of psychopathological networks – and derived graph theoretical measures such as centrality – is unclear (Epskamp, Borsboom, & Fried, 2016). For instance, it is unknown if a thicker edge weight between nodes A and B is significantly stronger than a somewhat smaller edge weight between nodes C and D, or if the centrality of node A is significantly larger than the centrality estimate of node B. To meet this challenge, we performed two main analyses using the novel R-package *bootnet*. First, we bootstrapped the 95% confidence intervals of the edge weights, providing an estimate about the accuracy of edges in the networks. Second, we examined the stability of the order of the centrality estimation by subsetting bootstrap (i.e. by dropping participants and re-estimating the network); if the order of centrality estimates from a network in which many participants were dropped is highly correlated to the order of the centrality from the original network, the centrality estimates can be considered stable. To this end, we also estimated the centrality stability coefficient (CS-coefficient); values should be at least 0.25 for the centrality to be stable, preferably above 0.5. Edge weight bootstrap was applied to both 20-item and 27-item networks, subsetting bootstrap only to the 20-item network (since we are only interested in centrality for this network). Further analyses and results are described in detail in the Supplementary materials. An R-tutorial paper on accuracy and stability for psychopathological networks that explains the above methods and metrics in more detail, along with their implementation in the R-package *bootnet,* is available elsewhere (Epskamp et al., 2016).

2.3.4. Visualization

Positive edges are printed in green, negative ones in red, and the stronger a connection, the thicker and more saturated it is. We use the Fruchterman-Reingold algorithm (Fruchterman & Reingold, 1991) that places nodes with stronger and/or more connections more closely together. We set the *maximum* edge value across all networks to 0.45, the strongest edge identified across networks. This means saturation and thickness of edges can be compared across networks (equally thick edges across networks have equal edge weights). We used a *minimum* value of 0.03 in all networks to enhance the interpretability of the graphs.

3. Results

3.1. Sample characteristics

Veterans ranged in age at the time of assessment from 21 to 89 years, the mean age was 54.0 years (SD = 14.8), and the majority (86.7%) were male and combat veterans (n = 107; weighted 54.0%). PCL-5 scores reflecting DSM-5 PTSD symptoms ranged from 4 to 80 (M = 31.0; SD = 13.4). A total of 61 veterans (weighted 26.2%) endorsed SI. Trauma exposures ranged between 1 and 15 events, with the average number of exposures being 6.0 (SD = 3.2); the traumatic events were on average 21.5 years ago (SD = 18.2 years, range 0–70 years). The three most commonly endorsed ‘worst’ traumatic events were: sudden death of close family member or friend (n = 49; weighted 24.8%); saw something horrible or was badly scared during military service (n = 28; weighted 16.0%); and suddenly abandoned by spouse, partner, parent, or family (n = 24; weighted 11.9%).

3.2. PTSD network

Fig. 1 shows a visualization of the network structure of the 20 DSM-5 PTSD symptoms. Overall, symptoms were positively connected within the network, and especially strong connections emerged between nightmares (B2) and flashbacks (B3), blame of self or others (D3) and negative trauma-related emotions (D4), detachment (D6) and restricted affect (D7), and hypervigilance (E3) and exaggerated startle response (E4).

The standardized estimates of betweenness, closeness, and node strength centrality are presented in Fig. 2; centrality estimates were substantially interrelated (correlation of 0.65 between node strength and closeness, 0.72 between node strength and betweenness, and 0.82 between closeness and betweenness). Due to these high inter-correlations, and because the order of strength centrality was estimated more reliably (see accuracy analyses below), we therefore focus our interpretation of the most relevant symptoms on node strength centrality in the remainder of the report.

The five nodes with the highest node strength centrality were negative trauma-related emotions (D4), detachment (D6), physiological cue reactivity (B5), flashbacks (B3), and emotional cue reactivity (B4), whereas the two least central nodes (with a substantial drop in node strength) were avoidance of thoughts (C1) and trauma-related amnesia (D1). This does not come as a surprise, considering that these two symptoms only exhibit few and weak connections (see Fig. 1).

3.3. PTSD network with clinical covariates

In a second step, we estimated the network structure of the 20 DSM-5 PTSD symptoms, with seven clinical covariates incorporated into the model. The resulting network is visualized in Fig. 3.

It is important to note once again that this graph can be understood as a partial correlation network: the associations are the ones left over when controlling for all other associations in the network. In this sense, edges between covariates and symptoms, for instance between suicidal ideation (SI) and self-destructive behavior (E2), are meaningful because they are not explained by the covariation among PTSD symptoms alone. Relevant associations emerged between covariates and symptoms (which can be interpreted as partial correlations) between self-destructive behavior (E2) and SI (0.25), between difficulty concentrating (E5) with anxiety (Anx; 0.13), depression (Dep; 0.12) and mental QoL/functioning (MFunc; −0.11), and between depression (Dep) with restricted affect (D7; 0.13). Of note, some of the covariates were substantially interrelated, including age with sex (-0.26), mental functioning (MFunc) with anxiety (Anx: −0.28) and depression (Dep: −0.24), depression (Dep) with suicidal ideation (SI: 0.39), and anxiety (Anx) with depression (Dep: 0.25).

3.4. Impact of covariates on the relations among symptoms

We also examined the impact of including the 7 covariates on the connections *among* PTSD symptoms (see Methods section). The resulting delta network (available in the Supplementary materials, Fig. S5) is nearly empty and features few very weak edges, with the strongest edge weight being only 0.06. This implies that connectivity among symptoms changes very little upon including the clinical covariates in the system. The sum of edges of the 20 symptoms was reduced from 8.7 to 7.7 once controlling for covariates; covariates “explain away” only about 11.5% of the connectivity of the PTSD symptoms. This conclusion is further corroborated by a very high correlation of 0.97 between the edge weights across the two networks (PTSD symptom network, and PTSD symptom network after controlling for covariates). In sum, the 20-item DSM-5 PTSD network is robust when other relevant variables are entered into the network and remains largely unaffected.

3.5. Network accuracy and stability

We estimated the accuracy and stability of the estimated networks. Results for the 20-item PTSD network are presented in Fig. 4. The edge weight bootstrap (Fig. 4a) revealed that the network is moderately accurately estimated: there is considerable overlap among the 95% CIs of edge weights, but especially the strongest edges are substantially stronger than many others. The subset bootstrap (Fig. 4b) showed that the order of node strength centrality is more stable than the order of betweenness and closeness. This is consistent with the CS-coefficient that was 0.36 for node strength, 0.05 for betweenness, and 0.13 for closeness. As described in the methods section, the coefficient should not be below 0.25, and preferably above 0.5, to obtain a stable order of centrality estimates. Further accuracy and stability analyses for this network are available in the Supplementary materials, including edge weights significance tests (testing for significant differences for all edges) and centrality difference tests (testing for centrality differences for all nodes).

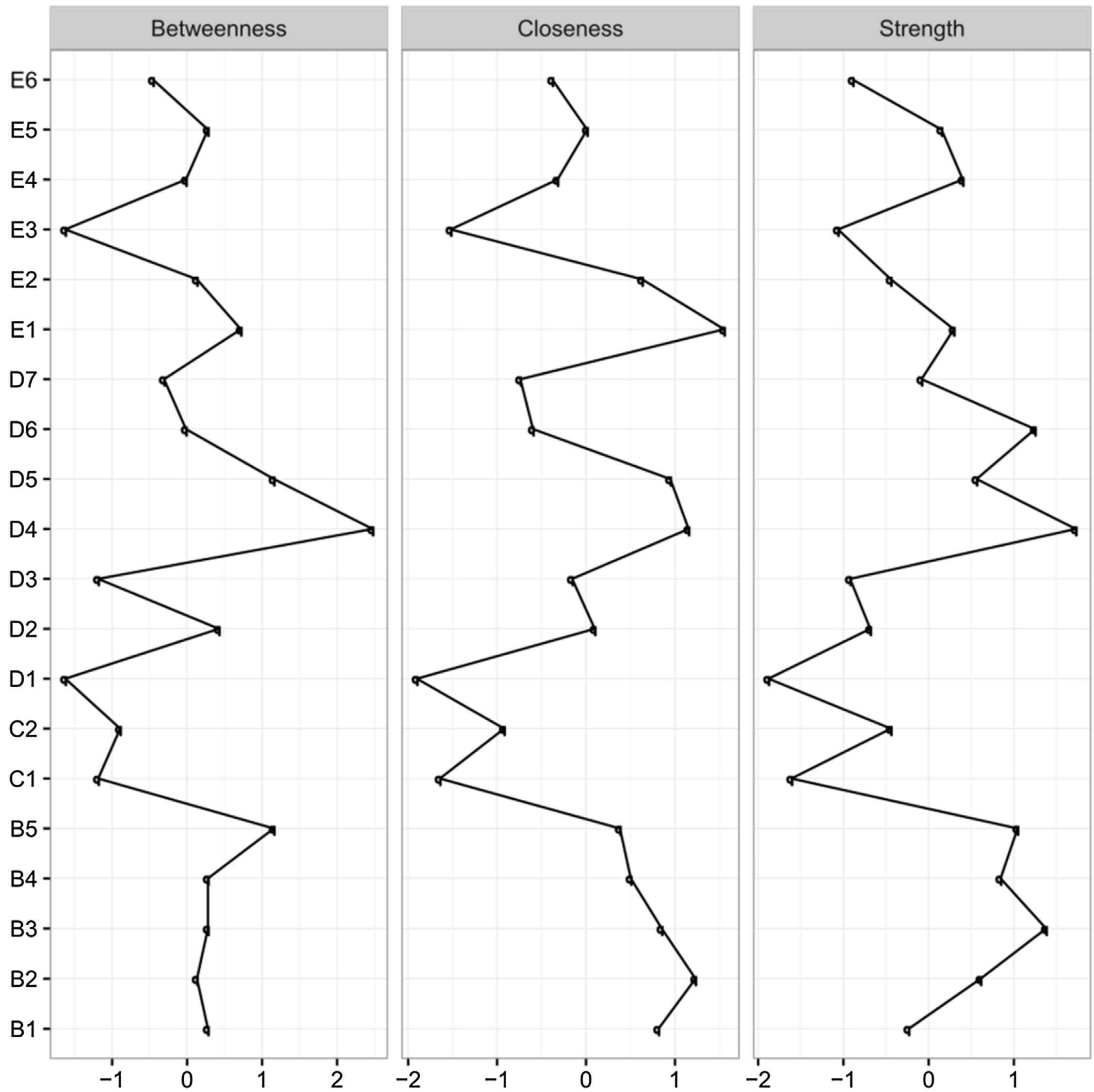

Fig. 2. Betweenness, closeness, and node strength centrality estimates for the 20 DSM-5 PTSD criterion symptoms. See Fig. 1 for symptom descriptions of the shortcodes.

For the 27-item network, moderate confidence intervals around the edge weights emerged, too. Further details are available in the Supplementary materials.

4. Discussion

To the best of our knowledge, the current study represents the first network analysis of DSM-5 PTSD symptoms (APA, 2013). We (1) analyzed PTSD Checklist-5 data from 221 individuals with clinically significant PTSD symptoms drawn from a representative sample of U.S. military veterans, (2) estimated the structure of two networks (a 20-item DSM-5 PTSD symptom network and a 27-item network adding seven clinical covariates), and (3) tested the robustness and stability of the networks. We believe these three unique features of the current study add to the small body of literature on PTSD symptom networks (McNally et al., 2015) and provide novel insights into the complex relationships between PTSD symptoms and clinically relevant correlates. In the following sections, we will first discuss connectivity between symptoms and symptom centrality in the PTSD network; and then connectivity between the PTSD network and clinical covariates.

4.1. PTSD network

In the current study, DSM-5 PTSD symptoms were generally positively connected among each other. The strongest edges in the network emerged between nightmares (B2) with flashbacks (B3); blame of self or others (D3) with negative trauma-related emotions (D4); detachment (D6) with restricted affect (D7); and hypervigilance (E3) with exaggerated startle response (E4). Of note, each of these connected symptom pairs as noted above co-occur within the network and therefore may appropriately belong to a particular symptom cluster within the DSM-5. However, some symptoms provided weak, and at times absent, connections with others from their respective DSM-5 symptom groups. For example, few connections were found between psychogenic amnesia (D1) and other symptoms from the NACM cluster (group D in Fig. 1). From a network perspective, the absence of a connection between two symptoms implies that they are conditionally independent of each other given the other symptoms in the network. If this finding were to generalize in other samples, it would raise doubts about whether psychogenic amnesia (D1) is indeed a good fit for the NACM symptom group. Our result is consistent with prior reports: repeatedly, weak factor loadings of psychogenic amnesia within the

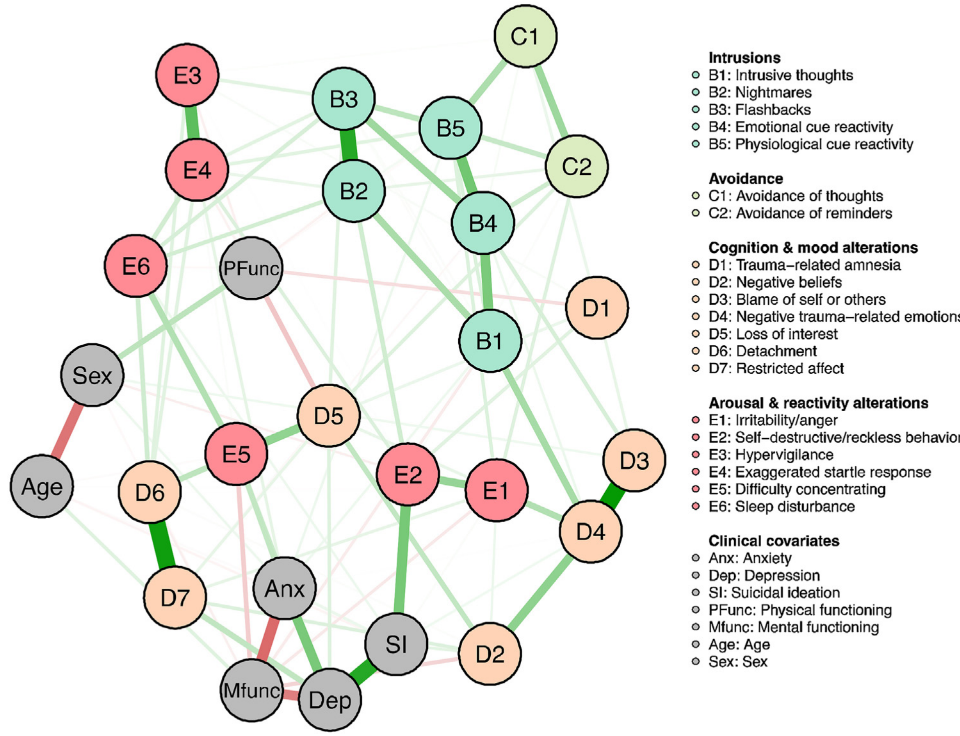

Fig. 3. Network containing the 20 DSM-5 symptoms of PTSD, along with 7 clinical covariates. Green lines represent positive associations, red lines negative ones, and the thickness and brightness of an edge indicate the association strength. For a color version of this Figure, we refer the reader to the online version of this paper. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

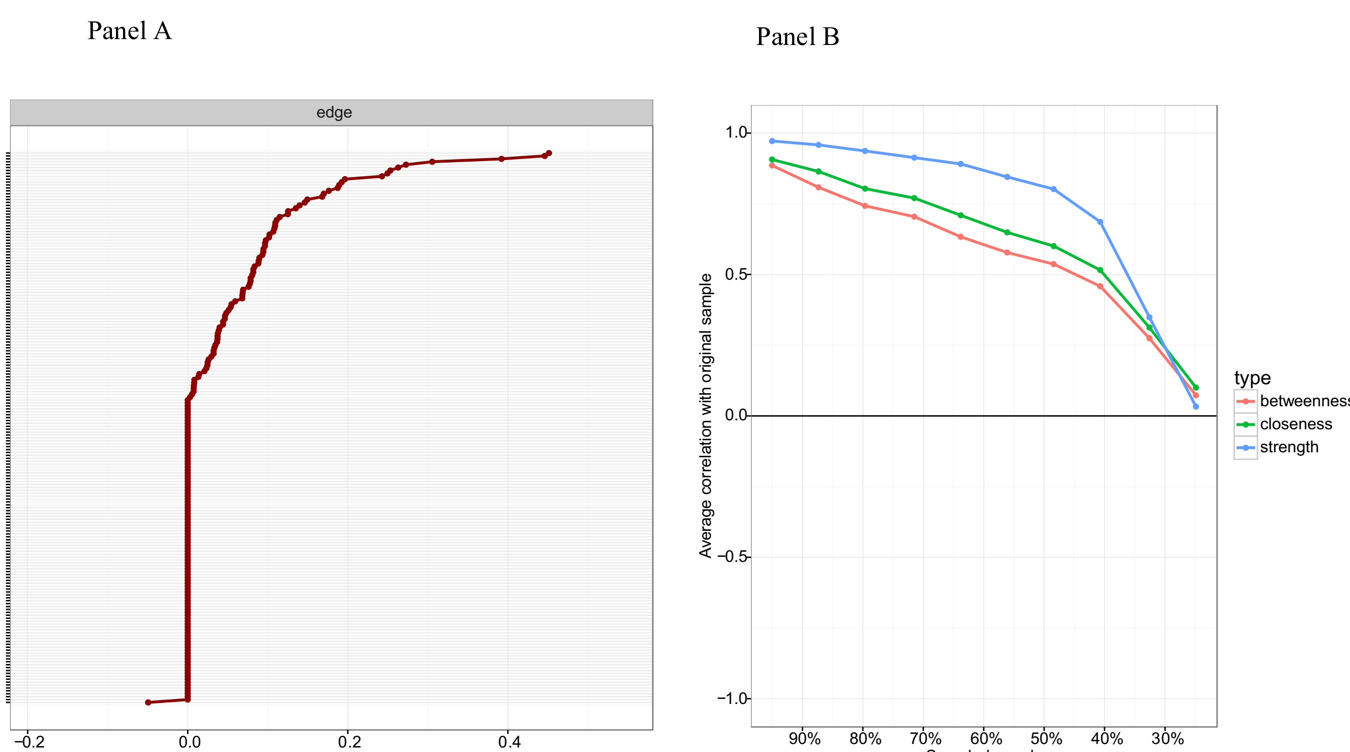

Fig. 4. Panel A: Bootstrapped confidence intervals (CIs) of the edge weights in the 20-item PTSD network. The red line indicates the edge weight values and the gray area the 95% CIs. Panel B: Subsetting bootstrap for the 20-item PTSD network that shows the average correlations between centrality indices of the original network constructed on the full data with networks estimated on samples with fewer participants. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

PTSD confirmatory factor analytic literature have emerged, which have led some researchers to question whether this item should be considered a core PTSD symptom (cf. Armour et al., 2016).

There were a number of similarities between our results, which analyzed DSM-5 PTSD symptoms and the only prior PTSD network analysis study, which analyzed DSM-IV PTSD symptoms (McNally et al., 2015). In both studies, strong associations were observed between hypervigilance (E3) and exaggerated startle response (E4) symptoms. Of note, McNally and colleagues also suggested that this association may be a self-reinforcing feedback loop. In addition, nightmares (B2) and flashbacks (B3) were strongly associated. These connections align with the clustering of PTSD symptoms as set out in both the DSM-5, given that hypervigilance (E3) and exaggerated startle response (E4) cluster in the alterations in arousal and reactivity symptom group (AAR), and nightmares (B2) and flashbacks (B3) are within the intrusions symptom cluster. Unlike McNally et al. (2015), we discovered additional associations with the two remaining re-experiencing symptoms of emotional (B4) and physiological cue reactivity (B5). Indeed, in our network, although the strength of connections varied, most re-experiencing symptoms were linked either directly or indirectly (through other symptoms [nightmare were linked to emotional cue reactivity (B4) through flashbacks (B3)]) with each other. This is also a notable finding given that the symptoms comprising the re-experiencing symptom group remained unchanged from the DSM-IV to DSM-5.

Blame of self or others (D3) and negative trauma-related emotions (D4) were highly connected in our network, and negative trauma-related emotions (D4) was connected, albeit to a lesser degree, with negative beliefs (D2). The connections between these symptoms are intuitive and may have relevance in the context of treatment planning. For example, cognitive processing therapy (CPT) is regarded as a highly effective way of treating chronic PTSD in veterans (Monsoon et al., 2006). CPT specifically targets thoughts, feelings, and beliefs about the PTSD precipitating traumatic event. Thus, if these symptoms are shown to be central to a PTSD network, the targeting of these symptoms within treatment planning could be particularly effective and should be investigated in future research. As we discuss in more detail in the limitations section, however, it remains to be seen whether central symptoms prove to be viable targets for psychotherapeutic intervention.

Assessing the robustness of symptom centrality revealed that the most central symptoms did not differ substantially from each other in their centrality, and should be considered roughly equally important. The most central symptoms were negative trauma-related emotions (D4), flashbacks (B3), detachment (D6), and physiological cue reactivity (B5), and we conclude that they may be of greatest clinical significance in U.S. military veterans. These symptoms differ considerably from the most central symptoms identified by McNally et al. (2015), who identified hypervigilance, concentration difficulties, and dreams about the trauma and future foreshortening as most central in their network model of DSM-IV PTSD symptoms. The fact that studies differ in the trauma populations under investigation (e.g., McNally et al. focused on PTSD symptoms related to a specific event [earthquake], while our sample focused on PTSD symptoms related to a broad range of traumatic events with the most common type of event being sudden death of close family member or friend and the third most common being abandonment) could explain the differences between studies, along with the use of DSM-IV vs. DSM-5 symptoms. Since PTSD symptom presentation can differ based on the precipitating traumatic event (Armour & Shevlin, 2010), it stands to reason that PTSD symptom networks and their associated findings may differ based on the index traumas of the sample under investigation. This has previously been shown for networks among depression symptoms, which can differ depending on precipitating life events such as romantic loss, stress, or losing a loved one (Cramer, Borsboom, Aggen, & Kendler, 2013; Fried et al., 2015).

4.2. PTSD network with clinical covariates

In extending our 20-item DSM-5 PTSD network, we added seven additional clinically relevant variables to the network. The strong association between self-destructive behavior (E2) and suicidal ideation (SI) is unsurprising given previous reports of self-destructive behaviors predicting males' SI (Hopes & Williams, 1999); prior research revealing that both thoughts of ending one's life and a previous suicide attempt significantly correlated with a diagnosis of PTSD in Vietnam veterans ($r = 0.53$, $p < 0.001$; and $r = 0.33$, $p < 0.001$, respectively; Kramer, Lindy, Green, Grace, & Leonard, 1994); and that out of six anxiety based psychiatric disorders, PTSD alone was significantly associated with suicidal ideation or attempts (Sareen, Houlaghan, Cox, & Asmundson, 2005). Of note, the self-destructive behavior item is a new addition to PTSD's nosology in the DSM-5, and our results suggest that this symptom may be a key contributor to SI risk in veterans. Some of the covariates in the 27-item network were substantially interrelated, the strongest of which was between depression and SI. While the causal direction of this association remains unclear, this link speaks to the possibility of a potential increased risk for suicidal ideation in trauma survivors displaying comorbid symptoms of depression and heightened self-destructive behaviors. The clinical implication of which may be the need for additional screening for SI in military veterans and other trauma survivors presenting with depression and/or heightened self-destructive behaviors. The relationship between depression and suicide has been previously reported with individuals experiencing depression being at a much greater risk of suicide than members of the general population (Kessler et al., 1994) and reports that approximately 2–7% of patients who are treated for depression die by suicide (Bostwick & Pankratz, 2000; Inskip, Harris, & Barraclough, 1998). Another strong association among clinical covariates was identified among depression and anxiety symptoms. This is consistent with several prior network studies reporting inter-relatedness of depression and anxiety symptoms (Boschloo et al., 2015; Cramer et al., 2010). A further notable finding was that concentration difficulties (E5) were connected with anxiety (Anx) and depression (Dep) symptoms, and mental QoL/functioning (Mfunc). Prior research has suggested that items such as concentration difficulties are not core symptoms of PTSD but rather reflect a more general distress component (Elklit, Armour, & Shevlin, 2010; Simms, Watson, & Doebbeling, 2002). The fact that concentration difficulties connect with multiple related constructs would support this viewpoint. Similarly, depression was found to be connected with restricted affect (D7). A recent study by Afzali et al. (2016) highlighted that several symptoms may have an important bridging role between PTSD and major depressive disorder (MDD). These authors identified both overlapping symptoms among PTSD and MDD (e.g., sleep problems and concentration problems), as well as unique symptoms (e.g., feeling sad and experiencing flashbacks) as central in the comorbidity network.

In summary, the network approach promises to offer novel insights into the comorbidity between PTSD and other conditions that may be clinically informative, and we are looking forward to the replication of prior work so that these findings can eventually be translated into clinical practice.

4.3. Conclusions and future directions

This study generates two intriguing questions; 1. Is the co-occurrence among PTSD symptoms better explained by a model of mutually reinforcing symptoms instead of the more commonly used factor models based on the common cause hypothesis?; and

2. Are these models mutually exclusive or could a trauma serve as the common cause for some symptoms initially that then mutually interact over time in a causal system (cf. Fried & Cramer, under revision)? Thus, the current study provides an extremely useful tool to generate hypotheses for follow-up studies.

Overall, the study provides further clarity in regard to how the DSM-5 PTSD symptoms relate to each other. Adding covariates to the network results in very little change in associations among PTSD symptoms, providing evidence that these connections can be considered fairly robust. An open research question is to what degree PTSD symptoms covary, and whether the DSM-5 symptom groups can be empirically substantiated. While the network approach merely understands such clusters as groups of elements that are somewhat more associated amongst each other, they play a crucial role in the DSM-5 given that diagnostic algorithms are directly linked to symptom groups. They determine who does and does not receive a diagnoses and in turn access to services; future analyses of the covariance among the clusters are hence of utmost importance to inform potential revisions of the DSM.

The identification of a group of highly connected symptoms (D2-D4) has a number of additional clinical implications. If it is known that certain symptoms are highly connected and central within a network, then these symptoms can be targeted in treatment planning. The alleviation of a highly connected symptom/s may ultimately break down the overall PTSD network and possibly help facilitate treatment gains. Future research should also endeavor to identify which symptoms drive the course of PTSD longitudinally. If these symptoms are targeted and alleviated, then this may help mitigate the often chronic nature of PTSD. In a similar vein, if certain symptoms within a PTSD network are identified as acting as key symptoms (known as bridge symptoms) leading to comorbid psychological disorders or behavioral outcomes of distress, then these symptoms can be targeted and alleviated to prevent comorbidity and/or adverse outcomes such as suicidal ideation, behavior, and attempts. In the current study, self-destructive behavior was identified as being associated with suicidal ideation, future studies of this nature should further explore this relationship, preferably by conducting finer grained analyses of the association between PTSD symptoms and multiple indicators of suicidal ideation and behavior. Additionally, these connections, both in a PTSD network and in one which additionally incorporates other related constructs and behaviors, should be assessed across a wide range of trauma populations to determine commonalities and differences depending on the index trauma. It would be of clinical relevance to know the manner of these connections in the index trauma of your patients as such would greatly facilitate treatment planning.

4.4. Limitations

The results have to be interpreted in the light of a number of limitations. First, the robustness analyses revealed that there was moderate uncertainty regarding the estimation of the edge weights and centrality parameters. This means that, for instance, while the few DSM-5 PTSD symptoms with the highest centrality estimates were very likely more central than the few symptoms at the lower end, we cannot properly distinguish which symptoms were more central among the top or among the bottom symptoms. The same holds for edge weights: while the confidence intervals of the strongest positive and negative edges do not overlap with the majority of moderately strong or weak edges, distinguishing clearly among the many moderately strong edges is not possible in our dataset. Future studies need to test more directly whether identifying strong edges and central symptoms proves insightful, for instance by testing whether breaking strong symptom connections and reducing central problems could turn out a viable strategy in psychotherapy and psychopharmacology.

Second, given that we utilized cross-sectional data it is impossible to ascertain directed influences among symptoms. Thus, it is unclear whether the most central symptoms activate other symptoms, are activated by other symptoms, or – mostly likely – whether both is the case. Third, our data was collected via a web-based, self-report assessment; future studies of this nature may wish to assess PTSD symptom networks from data collected via structured clinical interviews (Clinician-Administered PTSD Scale for DSM-5). Fourth, while the network approach follows the Research Domain Criteria (RDoC) set by the National Institute of Mental Health (NIMH) in assessing specific symptoms that can be considered distinct (endo) phenotypes, it would be interesting to capture more RDoC-relevant dimensions such as physiology, behavior and self-reports in future studies. Fifth, there are possibly many individual symptom networks dependent on the person and their particular trauma, and the present cross-sectional group-level analysis cannot uncover this type of heterogeneity (cf. Fried & Cramer, under revision). While network analysis in larger groups of traumatized individuals may provide a starting point to elucidate how PTSD symptoms relate to each other on average, it will be useful for future studies to focus on the idiographic aspects of trauma, which may lead to a personalized approach to understanding, monitoring, and treating PTSD symptoms. Sixth, there is evidence that the order in which items are presented to participants may impact on the relationships among items (Marshall, Schell, & Miles, 2013); it is thus important to consider possible item-order effects in both factor- and network-based analyses. Seventh, the current study assessed the PTSD network and associations pertaining to individuals who displayed clinically significant symptomatology, rather than, for example, the whole trauma exposed sample, which would have included those with little to no PTSD symptomatology. This more restrictive sampling led to comparably little statistical power when estimating the networks. For this reason, we applied the novel bootstrap routine to test the stability of the networks, and assessed covariates such as depression and anxiety as single nodes rather than examining covariance among individual symptoms of these constructs with the PTSD symptoms. Future research may endeavor to apply network analysis in larger clinical samples and examine comorbidity at the symptom level across a broader range of psychopathological constructs.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.janxdis.2016.11.008.

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