Title

Network Analysis of Neurobehavioral and Posttraumatic Stress Disorder Symptoms One Year
after Traumatic Brain Injury: A Veterans Affairs TBI Model Systems Study

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Abstract

Traumatic brain injury (TBI) is often experienced under stressful circumstances that can lead to symptoms of posttraumatic stress disorder (PTSD) and neurobehavioral symptoms of brain injury. There is considerable symptom overlap in the behavioral expression of these conditions. Psychometric network analysis is a useful approach to investigate the role of specific symptoms in connecting these two disorders and is well-suited to explore their interrelatedness. This study applied network analysis to examine the associations among PTSD and TBI symptoms in a sample of Service Members and Veterans (SM/Vs) with a history of TBI one year after injury. Responses to the Neurobehavioral Symptom Inventory (NSI) and PTSD Checklist-Civilian version (PCL-C) were obtained from participants who completed comprehensive inpatient rehabilitation services across five VA polytrauma rehabilitation centers. Participants ($N=612$) were 93.1% male with an average age of 36.98 years at injury. The analysis produced a stable network. Within the NSI symptom groups, the frustration symptom was an important bridge between the affective and cognitive TBI symptoms. The PCL-C nodes formed their own small cluster with hyperarousal yielding connections with the affective, cognitive, and somatic symptom groups. Consistent with this observation, the hyperarousal node had the second strongest bridge centrality in the network. Hyperarousal appears to play a key role in holding together this network of distress and thus represents a prime target for intervention among individuals with elevated symptoms of PTSD and a history of TBI. Network analysis offers an empirical approach to visualizing and quantifying the associations among symptoms. The identification of symptoms that are central to connecting multiple conditions can inform diagnostic precision and treatment selection.

Keywords: traumatic brain injury; posttraumatic stress disorder; Veterans; network analysis.

Introduction

Traumatic brain injury (TBI) is a priority focus within healthcare systems that serve Service Members and Veterans (SM/V).^{1–4} As the “signature injury” of Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn (OEF/OIF/OND), over 430,000 cases of TBI have been tracked by the TBI Center of Excellence since 2000.^{5,6} Moderate-to-severe TBIs are often managed within acute care and rehabilitation settings.⁷ However, the majority (80%) of TBIs among SM/Vs are mild (mTBI) and are often identified through screening mechanisms or during evaluation for co-morbidities such as pain or posttraumatic stress disorder (PTSD).^{6,8–10} Surveillance systems implemented across military health systems track outcomes, advance understanding of TBI, and plan for long-term comprehensive care for SM/Vs.^{11–14}

TBI and PTSD are common comorbidities among SM/Vs.^{8–10,15,16} In a systematic review of mTBI and PTSD, Carlson found a wide range of mTBI and PTSD comorbidity across studies—i.e., 0% to 89%; however, among large studies of OEF/OIF/OND SM/Vs, the rates of probable PTSD among participants with mTBI ranged from 33% to 39%.¹⁵ Both diagnoses have strong associations with other symptoms of physiological and psychological distress, including pain,^{8,17–20} substance abuse,^{21–23} anxiety and depression,^{24,25} and suicidal behavior.^{19,26–28} Due to extensive symptom overlap, distinguishing the unique contributions of these two conditions to overall symptom presentation remains a challenge. Behavioral manifestations of PTSD include symptoms that overlap with those commonly seen following TBI—i.e., depression/anxiety, insomnia, irritability/anger, trouble concentrating, fatigue, hyperarousal, and experiential avoidance.²⁹ Neurobehavioral symptoms of brain injury include fatigue, sleep problems, headaches, difficulty with concentration and memory, irritability, and changes in mood.^{30,31} With

uncomplicated mTBI, these symptoms typically resolve within three months, though the course of symptom evolution among SM/Vs varies.^{32,33}

It is difficult to determine whether neurobehavioral symptoms of TBI and symptoms of PTSD represent overlapping manifestations of distinct etiologies or they are part of a larger clinical syndrome secondary to a traumatic event involving injury.²⁹ Studies have compared patterns of post-concussive symptoms among military populations to those with and without posttraumatic stress,^{34,35} blast-related TBI,^{36,37} and to healthy controls.³⁶ In all studies, the presence of posttraumatic stress was associated with greater cognitive, somatic, and emotional post-concussive symptoms. However, Hoge et al. have argued that in the context of mTBI it is unhelpful to focus on assigning the manifestation symptoms to one etiology, as misattribution of symptoms to one condition or the other can result in stigmatization, inappropriate assessment, and misguided treatment.³⁸

Iverson has argued that neurobehavioral symptoms of TBI commonly shared across multiple psychiatric conditions such as depression and PTSD are best understood in a personal biopsychosocial context; in this model, symptoms and problems can be amplified and reinforced by vulnerability factors, environmental stressors, and psychosocial and personality factors.³⁹ Iverson recommends psychometric network analysis as a methodology to understand the associations among symptoms of TBI and PTSD as a syndrome in-and-of itself rather than necessarily attributable to distinct, underlying etiologies. Indeed, clinical research has benefitted from applying network approaches to various syndromes or to disentangle commonly comorbid symptomologies.^{40–43} One recent investigation provided network evidence that comorbid PTSD and depression have distinct network structures, identifying individual PTSD symptoms that

were highly influential (i.e., re-experiencing) within their own symptom communities but did not overlap with depression, thus providing PTSD-distinct targets for intervention.⁴⁴

Events such as head trauma—including repetitive injuries—often experienced under stressful circumstances can lead to both symptoms of PTSD and neurobehavioral symptoms of TBI. Given the challenge of distinguishing these overlapping symptoms, psychometric network analysis is well-suited to investigate how the symptoms of these two conditions are interrelated or can be mutually reinforcing. The current study applied network analysis to examine the associations among PTSD and TBI symptoms in a sample of SM/Vs one year after TBI.

Methods

Participants

This study used data from the Department of Veterans Affairs TBI Model Systems (VA TBIMS) longitudinal study.¹¹ Participants were recruited from five VA Polytrauma Rehabilitation Centers (PRCs) following comprehensive inpatient rehabilitation. The inclusion criteria for the VA TBIMS study were: (1) diagnosis of TBI per case definition (i.e., a traumatically-induced structural brain injury or physiological disruption of brain functioning due to external force, as evidenced by onset or worsening loss of and/or decreased consciousness, altered mental state, anterograde and/or retrograde amnesia, transient or stable neurological deficits, or intracranial lesion); (2) age ≥ 16 years at injury; and (3) admission to a PRC for TBI rehabilitation.

Procedures

Study procedures were approved by the Institutional Review Boards at each site. All participants in the VA TBIMS database provided informed consent either directly or by legal

proxy.¹¹ The study measures were collected directly from participants during a follow-up assessment by phone one year after injury.

Measures

The Neurobehavioral Symptom Inventory (NSI) is a 22-item self-report measure of persistent post-concussion symptoms after TBI. Individuals rate the severity of symptoms over the past two weeks, ranging from 0 (none; rarely present) to 4 (very severe; almost always present).⁴⁵ Analyses of the NSI factor structure have yielded various solutions; the 3-factor (cognitive, affective, and somatosensory/vestibular) and 4-factor (cognitive, affective, somatosensory, and vestibular) solutions have tended to be stronger and replicable.⁴⁶ The NSI has demonstrated strong internal consistency and acceptable test-retest reliability.⁴⁶ The Cronbach α among the current sample was .94.

The PTSD Checklist-Civilian Version (PCL-C) is a 17-item self-report measure of PTSD symptoms.⁴⁷ Individuals rate how much each symptom has bothered them over the past month, ranging from 1 (not at all) to 5 (extremely). Although the PCL-C has likewise been found to have various factor structures, the original *DSM-IV* three-factor model comprised of re-experiencing, avoidance, and hyperarousal symptoms has generally found broad support.⁴⁸ The PCL-C has demonstrated acceptable psychometric properties across trauma populations, including strong internal consistency.^{49,50} The Cronbach α for the full scale among the current sample was .98; the α s for the re-experiencing, avoidance, and hyperarousal subscales were .96, .94, and .93, respectively.

Analytic Approach

Psychometric network analysis is becoming a popular method to examine connections among individual symptoms as dynamic systems.⁵¹ In our application of this analytic framework,

nodes represented cross-sectional variables and *edges* represented the partial correlations between any two given nodes. Indices of centrality provide further information about the degree of influence a given node has in a network. *Strength* centrality refers to the overall influence of a node within a network (i.e., the absolute sum of all edges connecting to a given node). *Bridge* centrality provides an index of how well a given node connects specified node communities.

Nodes with high bridge centrality values play a pivotal role in connecting node communities which are either detected automatically by applying a selected algorithm or are determined manually (e.g., placing all PTSD symptoms into their own community and neurobehavioral symptoms in another). We coded node communities such that each of the three PCL factor score variables made up the PCL community, and each NSI item variable belonged to the respective somatosensory, cognitive, or affective symptom community; this three-factor structure for the NSI has been validated among veterans with TBI.⁵² We used a two-step index of expected influence (2EI) for bridge centrality estimates; this approach to bridge centrality produces estimates that indicate the extent to which a given node exerts influence on other communities directly and indirectly connected to their own.⁵³

To standardize time since injury, this study analyzed participant responses one-year post-injury using the raw values of the NSI items and the mean values of the PCL-C subscales as inputs to the network analysis. Given that our sample had a confirmed history of TBI, along with the opportunity to focus specifically on neurobehavioral symptoms, we elected to prioritize the NSI over the PCL-C by maximizing statistical power for item-level data with the former but subscale values for the latter. The sample size ($N = 612$) precluded the use of item-level responses to the PCL-C, as sample size must substantially exceed the number of estimated parameters to produce enough power to distinguish small coefficients consistently.^{54,55}

We estimated a psychometric network using the *estimateNetwork* function in the *bootnet* package for R version 4.0.2.⁵⁵ We used the EBICglasso regularization procedure for estimation which implements a machine learning algorithm and attempts to reduce the smallest edges in the network to zero while examining model fit, ultimately selecting the network that is the best fit.⁵⁶ Bridge centrality was estimated using the *bridge* function from the *networktools* package for R.⁵³ To examine network stability and accuracy we computed two 5,000-sample bootstraps (a case-dropping bootstrap and a nonparametric bootstrap) using the *bootnet* function from the *bootnet* package.⁵⁵ Pairwise deletion was used for missing values (see Table S1 for full missingness information).

Results

Characteristics of Sample

A sample of 612 TBIMS participants who had at least one PCL subscale score or one NSI item score were included in the current analyses due to the pairwise deletion approach used in the network analysis. Missing data rates were extremely low, ranging from 2.8-3.3% for PCL subscales and .7-1.1% for NSI items. Sociodemographic and injury-related characteristics appear in Table 1.

Table 1.

Sample characteristics (n=612).

Variable	<i>M (SD) or n (%)</i>
Sex (%)	
Male	567 (93.1%)
Female	42 (6.9%)
Race/Ethnicity	
Hispanic/Latino/Spanish	81 (13.7%)
White	468 (76.6%)
Black or African American	73 (11.9%)
Asian	27 (4.4%)

American Indian or Alaskan Native	29 (4.7%)
Native Hawaiian or other Pacific Islander	14 (2.3%)
Injury Severity (GCS Score)	
Mild (13-15)	191 (37.7%)
Moderate (9-12)	44 (8.7%)
Severe (3-8)	151 (29.8%)
Chemically Sedated	52 (10.3%)
Intubated	68 (13.4%)
Age at Injury	36.98 (16.14)
Time to Follow Commands (days)	9.37 (16.36)
Posttraumatic Amnesia (days)	30.96 (47.06)
Cause of Injury	69.07 (16.16)
Vehicular	307 (50.5%)
Gunshot Wound	25 (4.1%)
Assaults with Blunt Instrument	25 (4.1%)
Other Violence	84 (13.8%)
Sports	11 (1.8%)
Fall	115 (18.9%)
Hit by Falling/Flying Object	8 (1.3%)
Pedestrian	22 (3.6%)
Other	8 (1.3%)
Unknown	3 (.5%)

Network Analysis

Descriptive statistics (eTable 1) and zero-order correlations (eFigure 1) for the variables used in the current study are available as online supplements (<https://osf.io/agwj9/>). Correlation stability coefficients were ideal for edge weights ($CS = .60$) and bridge centrality ($CS = .44$); they were lower (though still acceptable) for strength centrality estimates ($CS = .28$). The edges in the network were largely stable, as only one edge in the network (connecting the “headache” and “difficulty making decision” nodes) was not included in the non-parametric bootstrap more than half (53.50%) of the time. Full edge weights and bootstrap estimates can be found in our supplemental materials (eTable 2).

The resultant network was relatively sparse (Figure 1). Single keywords from items defined each node, as seen in Figure 1. The centrality estimates, along with the item content associated with single keywords for each node, appear in Table 2. Within the NSI communities, the frustrated node (i.e., the NSI item “poor frustration tolerance”) was an important bridge node between the affective and cognitive TBI symptoms as it shared positive edges with three of the four cognitive nodes and yielded one of the strongest bridge centrality estimates in the network. Table 2.

Strength and Bridge Centrality Estimates from All Nodes in the Network.

Node	Abridged Item Content	Community	2EI	Strength
<i>Neurobehavioral Symptom Inventory (NSI)</i>				
Annoyed	<i>Irritability, easily annoyed</i>	Affective	0.86	1.06
Frustrated	<i>Poor frustration tolerance, overwhelmed</i>	Affective	1.06	1.14
Head	<i>Headaches</i>	Affective	1.25	1.04
Sad	<i>Feeling depressed or sad</i>	Affective	0.48	0.96
Sleep	<i>Difficulty falling asleep or staying asleep</i>	Affective	0.53	0.54
Tense	<i>Feeling anxious or tense</i>	Affective	0.40	1.16
Concentrate	<i>Poor concentration, inattentive, distracted</i>	Cognitive	0.93	1.36
Decide	<i>Difficulty making decisions</i>	Cognitive	0.49	1.02
Forget	<i>Forgetfulness, can't remember things</i>	Cognitive	0.79	0.91
Organize	<i>Slowed thinking, disorganized, can't finish</i>	Cognitive	0.67	0.96
Appetite	<i>Loss of appetite or increased appetite</i>	Somatosensory	0.75	0.80
Balance	<i>Loss of balance</i>	Somatosensory	0.18	1.47
Clumsy	<i>Poor coordination, clumsy</i>	Somatosensory	0.23	0.75
Dizzy	<i>Feeling dizzy</i>	Somatosensory	0.31	0.89
Fatigue	<i>Fatigue, loss of energy, tired easily</i>	Somatosensory	0.69	0.61
Hearing	<i>Hearing difficulty</i>	Somatosensory	0.07	0.45
Light	<i>Sensitivity to light</i>	Somatosensory	0.75	0.94
Nausea	<i>Nausea</i>	Somatosensory	0.46	0.78
Noise	<i>Sensitivity to noise</i>	Somatosensory	0.69	0.85
Numb	<i>Numbness or tingling on parts of the body</i>	Somatosensory	0.02	0.24
Taste	<i>Changes in taste or smell</i>	Somatosensory	0.14	0.77
Vision	<i>Vision problems, blurring, trouble seeing</i>	Somatosensory	0.17	0.68
<i>PTSD Checklist (PCL)</i>				
Avoid	<i>Avoidance Symptoms</i>	PCL	0.55	0.87
Hyp.Arousal	<i>Hyperarousal Symptoms</i>	PCL	1.22	1.46

Note. 2EI = two-step expected influence; Hyp. = Hyper; Re.exp = Re-experience.

taste/smell; nausea) node communities.

Figure 1. Psychometric network of TBI symptoms measured via the NSI and PTSD symptoms measured via the PCL. Blue edges indicate positive associations and red edges indicate negative associations. Edge width and depth of color indicates the strength of associations. Hyp. = Hyper;

Re.exp = re-experience. An interactive version of this plot can be examined in greater detail at <https://tbi-ptsd-network.netlify.app/>.

The three PCL nodes formed their own small cluster with the hyperarousal node yielding connections with the affective (i.e., feeling tense; irritable/annoyed; poor frustration; feeling sad; difficulty sleeping), cognitive (i.e., poor concentration), and somatic (i.e., sensitivity to noise) node communities. Consistent with this observation, the hyperarousal node had the second strongest bridge centrality in the network (Table 1). As such, PTSD symptoms comprising hyperarousal served as a crucial bridge among PTSD symptom and TBI symptoms. The avoidance node yielded an edge with the feeling sad node, whereas the re-experiencing node was only connected to the two PCL nodes. These findings suggest it is the affective symptoms of TBI and the affective content in hyperarousal that connect the clinical presentations/manifestations of TBI and PTSD.

Discussion

Neurobehavioral symptoms after TBI reflect complex interactions among cognitive, affective, and physical consequences of injury.⁵⁷ Network analysis permits an examination of these dynamic connections to better understand how individual symptoms contribute to their domain (or “community”) and how they overlap (or “bridge”) one domain to another. The current psychometric network analysis examined regularized partial correlations among four communities (i.e., cognitive, somatosensory, and affective symptoms from the NSI, and PTSD symptoms from the PCL-C), along with the relative contributions of individual symptoms within their assigned community and as bridging symptoms to other communities.

A key finding from these analyses was the connection between symptoms of PTSD and affective symptoms of TBI (e.g., feeling annoyed, frustrated, sad, or tense). Given the rates of

comorbidity between these two conditions, understanding the nature of overlapping symptoms is important, and the presence of affective distress might influence providers to focus on one diagnosis at the expense of the other. Such clinical confusion may be likeliest to occur when the frequency or intensity of affective symptoms are driving elevated total scores on measures like the PCL-C and NSI. Within the community of PTSD nodes, re-experiencing and avoidance symptoms were relatively isolated from the symptoms of TBI. The relative lack of edges between the re-experiencing and avoidance nodes and those outside of the PTSD community is consistent with the well-established structure of the PTSD construct and supports clinical judgment that prominent experience of these symptoms is likely indicative of posttraumatic stress irrespective of whether there is a concurrent TBI. When such distinctions are possible, they can inform the selection of an empirically supported intervention for PTSD, such as Cognitive Processing Therapy or Prolonged Exposure.^{58–63}

Hyperarousal was a crucial bridge between symptoms of PTSD and TBI, suggesting hypotheses for future investigations of its role in connecting these two diagnoses and as a potential target for intervention. First, among SM/Vs with a history of TBI, hyperarousal could accentuate the experience of neurobehavioral symptoms, much as individuals with anxiety sensitivity tend to experience increased fearfulness or awareness of somatosensory symptoms.^{64,65} Second, given the association between hyperarousal and facets of irritability (e.g., feeling annoyed, frustrated, tense), hyperarousal might contribute to a cascading effect through the communities of TBI symptoms. Such downstream connections with cognitive symptoms could occur despite the modest number of direct connections between the cognitive TBI symptoms and hyperarousal. For example, the frustrated node, which shares an edge with

hyperarousal, also shares edges with difficulty getting organized and difficulty making decisions—neither of which share an edge with hyperarousal.

Overall, hyperarousal appears to play a key role in holding together this network of distress through connecting posttraumatic stress and neurobehavioral symptoms of TBI. As such, hyperarousal could be an important target for intervention research among individuals with elevated symptoms of PTSD and a history of TBI. Although clinically intuitive, future research could clarify the conditions under which it is helpful to introduce strategies to reduce hyperarousal early in the course of treatment for either PTSD or TBI; given its role in the network of symptoms shown with the current data, addressing hyperarousal early could help to make other symptoms of PTSD and TBI more responsive to treatment. Fortunately, hyperarousal is readily amenable to cognitive-behavioral (e.g., psychoeducation; diaphragmatic breathing) or mindfulness-based interventions.^{66–69} Such interventions offer opportunities to disrupt these mutually reinforcing symptoms; they are face-valid, offer quick symptom reduction, and can serve as an entry into a holistic approach to care.

Although the PTSD and TBI communities were almost exclusively connected through hyperarousal and affective symptoms consistent with “irritability,” (e.g., tension, frustration, annoyance), there was one connection between avoidance and feeling sad. Compared to irritability, sadness represents an emotional state associated with lower arousal; this finding was accentuated by the negative edge shared by sadness with hyperarousal. For SM/Vs with elevated symptoms of PTSD whose presentation is more consistent with low arousal (vs. hyperarousal), clinicians might consider facilitating a therapeutic approach designed to target experiential avoidance through interventions such as prolonged exposure or acceptance and commitment

therapy. Future applications of psychometric network analysis that include symptoms of depression along with PTSD and TBI could further characterize these associations.

Limitations of Data and Analyses

Network analysis has been applied in diverse fields, yet its application to psychological research is relatively new; as such, its limitations in this area are still being explored.⁷⁰ The current sample size compelled a reduction in the number of PCL-C nodes by using subscale means instead of item-level data to conserve statistical power. A much larger sample size would have allowed the use of item-level data for the PCL-C, potentially resulting in more granular results. Sample size also influences the stability of the network and the estimation of edges, both of which increase along with sample size.⁵⁵

Because the NSI and PCL-C data were cross-sectional, the results might erroneously imply a static relationship among nodes when they actually change over time or have some other dynamic component. This is a limitation of network analysis diagrams in general.³⁹ Further, when responding to the PCL-C, participants were not instructed to reference a specific stressor. Whether symptoms of posttraumatic stress are related to TBI or another stressful experience is unknown; nonetheless, the network analysis provides information about the associations among concurrent symptoms irrespective of the index trauma. The current analysis did not examine directionality, only strength of association. As such, these findings may be useful to generate hypotheses about causal relationships, and future studies might emphasize directional interactions as well as temporal ones.⁵⁴

Important non-symptom variables were absent from the network that could influence both TBI and PTSD—e.g., age and gender.^{71,72} Including non-symptom nodes could transform the results of the network and warrants further exploration.⁷³ Finally, the relative homogeneity of

the participants in the VA TBIMS—predominantly male and White—precludes the results generalizing to larger, more heterogeneous TBI populations, despite their implications for SM/Vs.¹³

Conclusion

The current study is among the first to perform a network analysis of neurobehavioral and PTSD symptoms as reported by individuals with TBI, and the first to examine this symptom network in a military cohort. Symptom overlap between these commonly co-occurring conditions posed challenges for diagnosis and treatment. As demonstrated herein, network analysis offers an empirical approach to visualizing and quantifying the relationships among symptoms that can improve diagnostic precision, identify treatment targets, and inform treatment selection. Future extensions of these methods to include a broader range of symptoms experienced by individuals with TBI may yield novel insights into the ways in which co-occurring symptoms can serve to mutually exacerbate or maintain ongoing health problems in this population.

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