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Research paper

Age-related differences in borderline personality disorder symptom networks in a transdiagnostic sample

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ABSTRACT

Background: Naturalistic longitudinal studies of Borderline Personality Disorder (BPD) indicate that symptoms improve over time. In the present study, we applied network theory to the question of how BPD symptom networks may differ as a function of age.

Methods: In a transdiagnostic sample of 5,212 patients presenting for acute psychiatric treatment, we administered a measure of BPD symptoms and then used a novel machine learning technique to test the hypothesis that symptom networks would significantly differ across the age of participants.

Results: Results supported two significant differences in the BPD symptom network that emerged at age 46. In older participants, the relationships among symptoms of non-suicidal self-injury/suicide and emptiness was weaker, yet the relationship between anger and relationship problems was stronger. No differences emerged for relationships between all other symptoms.

Limitations: Given the cross-sectional nature of this study, the potential influence of cohort effects cannot be ruled out.

Conclusions: These findings support the utility of network theory for elucidating potential pathways by which the relationships between symptoms of BPD may differ as a function of age in treatment-seeking individuals. In parallel, results of this study support the highly central role of strong emotions in BPD regardless of age.

1. Introduction

Borderline Personality Disorder (BPD) is a severe psychiatric disorder marked by symptoms including affective instability, impulsive and self-destructive behaviors, and identity disturbance (American Psychiatric Association, 2013). Although diagnostic criteria for personality disorders emphasize stability of symptoms over time, numerous studies show that individuals with BPD report significant symptomatic improvement over long-term follow up (Paris et al., 1987; Soloff and Chiappetta, 2019; for review, see Temes and Zanarini, 2018). Given the high rate of impairment linked to symptoms of BPD, researchers have sought to understand why symptoms appear to improve over time for many individuals with this diagnosis. Certain predictors such as higher IQ, less psychiatric comorbidity, and better initial psychosocial functioning appear to be associated with favorable outcomes over long-term follow-up (Soloff and Chiappetta, 2018; 2019; Zanarini et al., 2018). Longitudinal data also indicates that some symptoms such as non-suicidal self-injury (NSSI) and affective instability diminish relatively quickly, while other symptoms including anger and emptiness may persist for longer intervals (Zanarini et al., 2007).

Longitudinal studies have yielded inconclusive evidence about whether improvements in symptoms can be explained by the passage of time as opposed to differences in the age of individuals in the study (Álvarez-Tomás et al., 2019; Shea et al., 2009; Soloff and Chiappetta, 2018). However, the possibility of age-driven decreases in symptoms is supported by findings indicating that BPD-relevant symptoms change as a function of age across psychopathology: for example, both impulsivity and aggression are more strongly related to completed suicides in younger vs. older individuals (McGirr et al., 2008), and the prevalence of substance use disorders decreases with older age (Compton et al., 2007).

Network theory of psychopathology is one potential way to understand significant changes in the trajectory of BPD symptoms over time.

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According to network theory, clinical syndromes arise from causal interactions between symptoms in a network (Borsboom & Cramer, 2013; Fried et al., 2017). For example, in the context of BPD, affective instability could potentially lead to other symptoms such as dissociation to manage unbearable emotions, which may then lead to emptiness. Network analysis allows for an empirical test of how such individual symptoms, or "nodes," relate to other symptoms in a network. Nodes with the highest *centrality* in a network are those that are most highly connected to other nodes.

Evidence supporting network approaches to psychopathology has rapidly increased (Fried et al., 2017), including recent studies highlighting network approaches to understanding core symptoms of BPD. In one study, symptom nodes of affective instability, identity disturbance, and efforts to avoid abandonment showed the highest centrality across a combined sample of university students and adults seeking psychiatric treatment (Richetin et al., 2017). More recently, Southward and Cheavens (2018) tested symptom networks of BPD in a large sample of students and treatment-seeking adults, as well as testing network differences between those with higher vs. lower BPD symptom levels. Those in the high symptoms group showed central nodes of loneliness, impulsivity, and intense moods; in contrast, the low-symptom group showed central nodes of emptiness, intense moods, and mood instability.

Despite these recent advances in applying network theory to BPD symptoms, prior studies have not tested how BPD symptom networks differ by age. Given its focus on symptom-symptom relationships, network analysis is the ideal method to test if the associations between symptoms change as a function of age, which would potentially suggest that changes in symptom relationships may help explain changes in symptom severity. In contrast, if relationships between symptoms remain stable across age groups, this would suggest that other explanations aside from interactions between symptoms are more likely to contribute to changes in symptom severity seen over time in naturalistic longitudinal studies.

In the present study, we expanded on previous investigations by first examining the network of BPD symptoms in a large, transdiagnostic clinical sample of adults presenting for partial hospitalization in a psychiatric hospital. Although we did not focus on individuals diagnosed with BPD, we reasoned that many of the common features of BPD, such as neuroticism, affective instability, and difficulties regulating emotions, are transdiagnostic in nature, and thus, are important to characterize in both those with formal BPD diagnoses as well as the broader spectrum of psychopathology (Ebner-Priemer et al., 2015; Samuel and Widiger, 2008; Sloan et al., 2017; Widiger and Oltmanns, 2017). We then used a novel machine learning technique to examine changes in symptom networks across the age of participants. We predicted that age would significantly moderate the symptom network of BPD, such that these networks would differ between older and younger individuals. Given the exploratory nature of these analyses we did not predict a specific age at which the networks would diverge or how the networks would diverge. We predicted that affective instability would emerge as a central symptom node across all ages, based on prior network analyses of BPD symptoms (Richetin et al., 2017; Southward and Cheavens, 2018).

2. Methods

Participants in the present study were patients presenting for treatment at a partial hospitalization program (PHP) for adults (18+) with psychological disorders. Data were collected from 07/2010 to 10/2018. All data were collected as part of routine clinical care. We obtained a deidentified dataset, and the local Institutional Review Board deemed this analysis as exempt. Individuals receiving treatment in the program present with range of psychiatric diagnoses, most commonly mood, anxiety and personality disorders (for detailed description of the setting and patient population, see Forgeard et al., 2018). Measures were administered to participants on the day of admission to the partial hospital program. Participants completed measures as part of clinical progress monitoring administered using REDCap (Harris et al., 2009).

2.1. Measures

McLean Screening Instrument for Borderline Personality Disorder (MSI-BPD, Zanarini et al., 2003). The MSI-BPD is a brief screening measure for symptoms of borderline personality disorder. This scale assesses all nine symptom criteria for BPD based on DSM-IV criteria; it includes two questions assessing dissociation and paranoia independently, resulting in ten total items (Zanarini et al., 2003). Some items include multiple behaviors within the same item; the "Self-Injury/Suicide" item assesses both NSSI and suicide attempts. Items are rated on a binary "yes/no" scale and are summed to result in a total score from zero to ten, with higher scores reflecting more symptoms endorsed. Previous studies have established the reliability and validity of this measure, including determining a recommended cutoff score of seven or higher to indicate the possible presence of BPD (Gardner and Qualter, 2009; Zanarini et al., 2003). In the present study, 1364 patients (27.7% of the sample with complete MSI-BPD data [n = 4923]) met this threshold for possible diagnosis of BPD, and the internal reliability of the measure in this sample was acceptable (α = 0.74).

2.2. Analyses

Preparation and network generation. Missing data (2% of total observations) was handled using multiple imputation with the *mice* package (van Buuren and Groothuis-Oudshoorn, 2011). We estimated networks using the graphical least absolute shrinkage and selection operator (GLASSO) method, which estimates regularized partial correlations between nodes. The use of GLASSO shrinks small edges in the network to 0, which helps to deal with the problem of multiple testing (i.e., reducing false positive errors). Correlation matrices were initially estimated using a Pearson's phi coefficient before applying the EBIC-glasso procedure using the *qgraph* R package (Epskamp et al., 2012). We used the default hyperparameter value (*gamma* = 0.5) for regularization. For centrality analyses, we used expected influence centrality (Robinaugh et al., 2016), and used bootstrapping to ensure the stability of parameters (Epskamp et al., 2018).

We used multidimensional scaling (MDS) to plot the layout of the networks (see Jones et al., 2018 for a tutorial). This plotting approach is useful because unlike in most network plots, nodes with stronger similarities in terms of edge weights are plotted more closely together. When using this approach, intuitive spatial inference of node positions better matches the actual structure of the network. Distances in the MDS layout reflect the similarities between nodes approximately, due to the constraints of plotting in a two-dimensional space. The *stress-1* value of the MDS fit can be used to guide interpretations (Mair et al., 2016).

Network analyses is based upon the premise that each node in the network represents a unique construct. If two nodes in a network measure the same underlying construct, this can result in an inflated correlation between the two nodes and also interferes with inference in the partial correlation matrix. To test for this possibility, we used the goldbricker function (Jones, 2018), which tests for topological overlap between nodes.

Partitioning with *networktree*. Network models computed across an entire sample are limited by assumptions of homogeneity. Because each edge is computed across the entire sample, important distinctions that exist within subgroups of the sample may be disguised or hidden. In some cases, the population parameter does not meaningfully reflect any subgroup, but rather an average across widely differing subgroup parameters. In our case, we were interested in whether networks of BPD symptoms were heterogeneous across age groups. In other words, we wanted to test whether the associations between BPD symptoms were

different depending on age, and if so, identify which age groups specifically were different from one another. We used model-based recursive partitioning implemented in the *networktree* R package (Jones et al., 2019a, 2019b). Model-based recursive partitioning is a semi-parametric approach that searches for possible heterogeneity in network structures. If heterogeneity is found, the algorithm identifies optimal split points in the data based on chosen covariates to produce a tree-like structure. At the bottom of the tree is a network model for each partition. The *networktree* function uses a correlation matrix to optimize splits; further procedures such as GLASSO can be applied to the terminal models after the partitioning is complete. We used an alpha threshold of $p = .05$ and a BIC pruning approach to reduce the incidence of spurious partitions.

Network comparison tests. The *networktree* function generates splits that maximize heterogeneity in network parameters across groups and tests for statistical significance across each split. It can tell us whether BPD networks differ by age, and at what specific age groups. However, *networktree* only provides a global test of heterogeneity in the entire network; it does not test for the significance of differences across *specific edges* in the network. It also does not test for differences in the *density* of the network (viz., *global expected influence*; the sum of all edge weights, signifying the total amount of positive connectivity between nodes). Therefore, after partitioning our data with *networktree*, we used a permutation test via the *NetworkComparisonTest* framework (van Borkulo et al., 2017) to test for differences in each edge and for differences in the global expected influence across each age group. We used the False Discovery Rate (FDR) correction for multiple comparisons and a threshold of $p = .05$ post-correction (Benjamini and Hochberg, 1995). The permutation test returns a level of significance but cannot give an estimate of effect size. Thus, in addition to the permutation test, we employed a bootstrapped network comparison to generate an effect size confidence interval. Considering that not all partitions of data have the same sample size, the bootstrapping method also has another advantage – in each bootstrapped iteration, random samples can be drawn such that the sample sizes are equal across partitions for each comparison. This reduces concerns regarding the influence of sample size on network comparisons.

3. Results

3.1. Sample description

The current sample ($N = 5212$) included 2834 (54.3%) females and 2378 males (45.6%). The average age was 34.4 years (SD = 13.86, range: 17 to 78). The majority of participants identified as non-Hispanic (95.9%) and the predominant reported race was White (88.1%), in addition to more than one race (3.4%), Asian (2.2%), unknown (1.4%), Black (1%), other (0.7%), American Indian (0.4%), or Hawaiian or Pacific Islander (<0.1%). Average score on the MSI-BPD was 4.66 (SD = 2.64), with significantly higher scores among females ($M = 4.91$, $SD = 2.61$) than males ($M = 4.38$, $SD = 2.64$), $t(4752) = 7.09$, $p < 0.0001$. There was a small yet significant negative correlation between MSI-BPD score and age, $r = -0.19$, $p < 0.0001$.

3.2. Main analysis

We used the *networktree* algorithm to test whether networks of BPD symptoms would differ by age. We found an optimal split at the age of 46, such that networks of individuals of age 46 or younger differed from networks of individuals above age 46. The results of this analysis are presented in Fig. 1. The *networktree* algorithm ensures an optimal split according to the entire model but does not test for individual parameter differences or global expected influence across the two networks. For this, we used a permutation test via the *NetworkComparisonTest* framework. The global expected influence was slightly higher in the younger group but did not significantly differ across the two groups (*GEI* = 3.44, 3.29, $p = .18$). After correcting for multiple testing, we found two significant edge differences in the networks. First, the relationship between the nodes "angry" and "relationship" was stronger in the older group ($r = 0.23$, 0.11, $p < .001$). Second, the relationship between "empty" and "suicide" was weaker in the older group ($r = 0.00$, 0.10, $p < .001$). Using bootstrapping, we were able to estimate effect sizes for each of these edge differences while constraining the sample sizes to be equal in each bootstrapped sample, indicating a small change in the regularized partial correlation values ("angry/relationship," $\Delta r = 0.12$ [.04, 0.20]; "empty/suicide," $\Delta r = -0.09$[1] [−0.14, −0.03]).

The group of individuals 46 and younger was larger than the group older than 46 ($n = 4012$, vs. 1200). Among those who had complete MSI-BPD data, a relatively larger proportion of individuals 46 or younger met the clinical cutoff (30.3%, $M = 4.9$, $SD = 2.6$) compared to the proportion among individuals over 46 (18.7% $M = 3.8$, $SD = 2.5$), $p < .0001$. As noted earlier, there was a small yet significant negative correlation between MSI-BPD score and age, $r = -0.19$, $p < .0001$.

Expected influence centrality remained relatively consistent across the full sample and in both age subgroups (see Fig. 2). Among the most central symptoms were "moody," "angry," and "distrustful." The "suicide" item had consistently lower centrality compared to other items. The stability of expected influence was excellent in the full sample and within both age groups (CS coefficient ≥ 0.75). Figures displaying difference tests between different items can be found in the supplemental materials.

3.3. Sensitivity analyses

We conducted two sensitivity analyses in reference to the *NetworkComparisonTest* to ensure the robustness of our results. First, we conducted the test across the two groups using partial correlation networks (i.e., without regularization). The partial correlation networks indicated the same results as our GLASSO networks: significant differences were found after FDR corrections for the edges "angry/relationship" and "empty/suicide" in the same directions as before, and no significant difference was found for global expected influence. Effect sizes were similar, indicating that shrinkage had a minimal effect ("angry/relationship," $\Delta r = 0.13$ [.05, 0.21]; "empty/suicide," $\Delta r = -0.10$ [−0.18, −0.03]). We conducted a second sensitivity analysis using Ising models rather than GLASSO. The Ising model comparison also returned identical results, with significant differences after FDR corrections for the edges "angry/relationship" and "empty/suicide" in the same directions and no significant differences in global expected influence.

We used the *goldbricker* function to test for the possibility that nodes in the network were redundant measures of the same underlying construct. The *goldbricker* function works by comparing the topological overlap between nodes; that is, the degree to which any two nodes share similar correlations with the rest of the network. If two nodes have near-identical correlation patterns with the rest of the network, this increases suspicion that they are redundant measurements. We used a threshold of 75% overlap (i.e., less than 25% of significant differences, $p = .001$) to select potentially overlapping nodes. The topological overlap analysis between nodes in *goldbricker* indicated that no redundant nodes were present in our dataset. We used an MDS plotting approach based on the full sample to position nodes. This layout indicated an acceptable level of fit (*stress-1* = 0.15).

At the request of a reviewer, we incorporated sex as a variable in the *networktree* algorithm to determine whether significant splits would be found between males and females. When testing for both sex and age splits simultaneously, only a split between age was found (identical to our main analysis). When using sex as a sole split variable (i.e., not

[1] Note that the bootstrapped effect size can vary slightly from the invariance from the estimated networks.

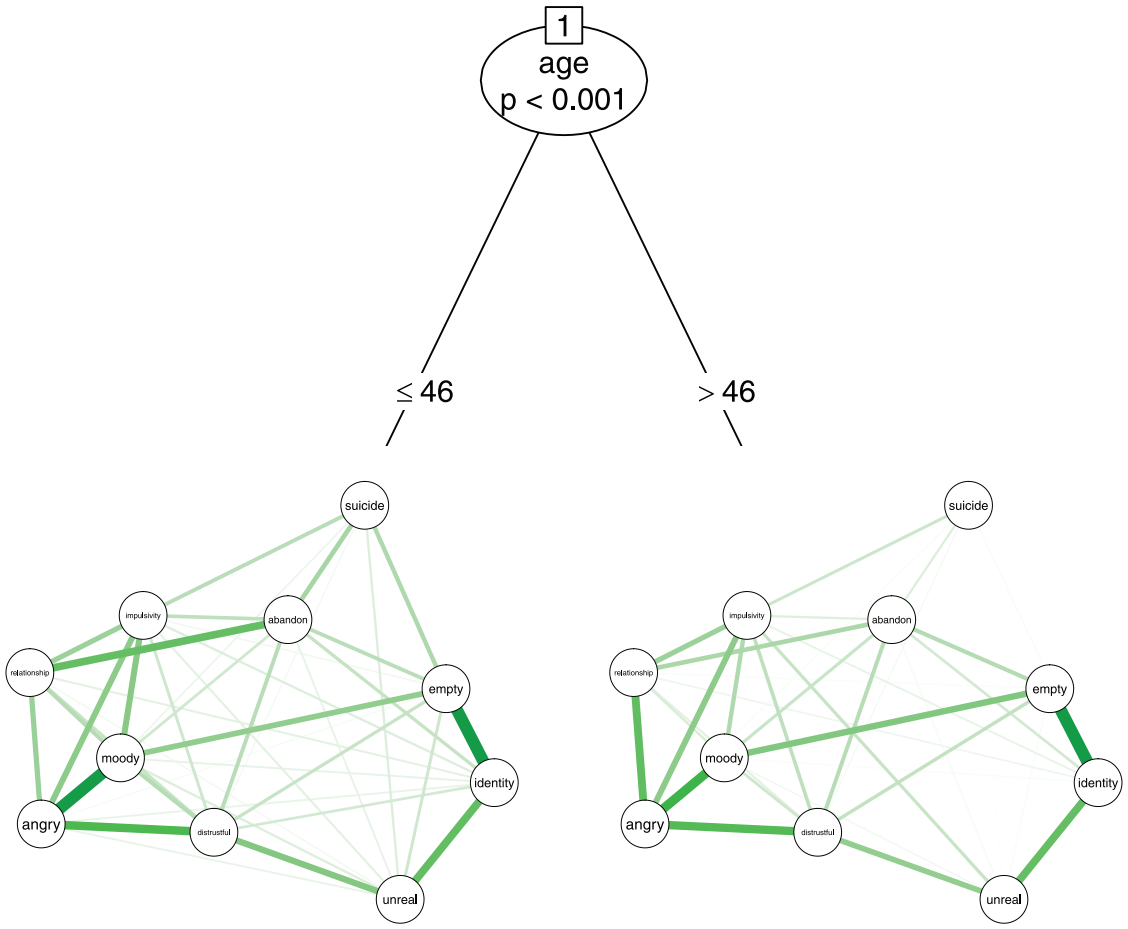

Fig. 1. Networktree by Age. Results of the networktree analysis shows that symptom networks of individuals of age 46 or younger differed from networks of individuals above age 46. Circles represent individual symptoms from the 10 questions on the MSI-BPD measure, and lines reflect the strength of the relations between symptoms, with thicker lines indicating stronger relationships.

testing for differences in age), no significant splits were found. This indicates that networks did not significantly differ by sex in our sample.

4. Discussion

Results of this study indicate that the symptom networks of BPD differ as a function of patient age in a large, transdiagnostic, treatment-seeking sample. Specifically, we identified a weaker link between emptiness and NSSI/suicide attempts among the older group, yet also a stronger link between anger and relationship problems in the older group. These findings are consistent with longitudinal studies documenting relatively fast remission of NSSI and suicidal behavior as compared to longer-term problems with anger (Zanarini et al., 2007). In addition, these findings indicate that network theory may help explain results of these previous longitudinal studies, in showing that the causal relationships between symptoms may differ as a function of age. Given the cross-sectional nature of this exploratory study, this theory could be tested in future studies using longitudinal methods.

Results of this study provide mixed evidence for how the relationships between symptoms may differ based on age. The symptom networks of BPD were significantly different for those younger vs. older than the mid-40s, which is highly consistent with previous research indicating significant differences in certain symptoms and comorbid disorders at age 45 among adults with BPD (Morgan et al., 2013). Notably, population-based studies of BPD symptoms have also identified the mid-40s as a point at which the prevalence of this disorder declines (Grant et al., 2008). However, as described in more detail below, certain symptoms showed stronger relationships among each other, while other symptoms showed weaker relationships. Thus, results are not consistent with the idea that symptomatic improvements in older age are a result of weaker causal relationships among all types of symptoms. Of note, these findings are based on a treatment-seeking transdiagnostic sample; weaker relationships between all types of symptoms may be more characteristic of non-treatment-seeking samples.

One strength of the present study is the use of a large, treatment-seeking clinical sample. An additional strength is the use of sensitivity analyses and corrections for multiple testing to guard against potential spurious associations. Although previous network analyses of BPD symptoms have included samples comprised of a mixture of clinical and non-clinical participants, this study is to our knowledge the first investigation of BPD symptom networks in a solely clinical sample. Results of this study support the highly central role of strong emotions in BPD regardless of age: the item with the prompt “extremely moody” was among the most central, similar to previous studies reporting central symptoms involving affective intensity and lability (Richetin et al., 2017; Southward and Cheavens, 2018). In contrast to these previous studies, we also identified anger as one of the most central symptoms. Anger is increasingly recognized as an important transdiagnostic symptom (Fernandez and Johnson, 2015), and the present study reflects its importance in a large treatment-seeking sample.

The predominant limitation of the present study is its cross-sectional nature. We cannot rule out the influence of cohort effects, nor can we claim that the symptom networks of BPD change over time. Related to this limitation, recent longitudinal studies indicate that many

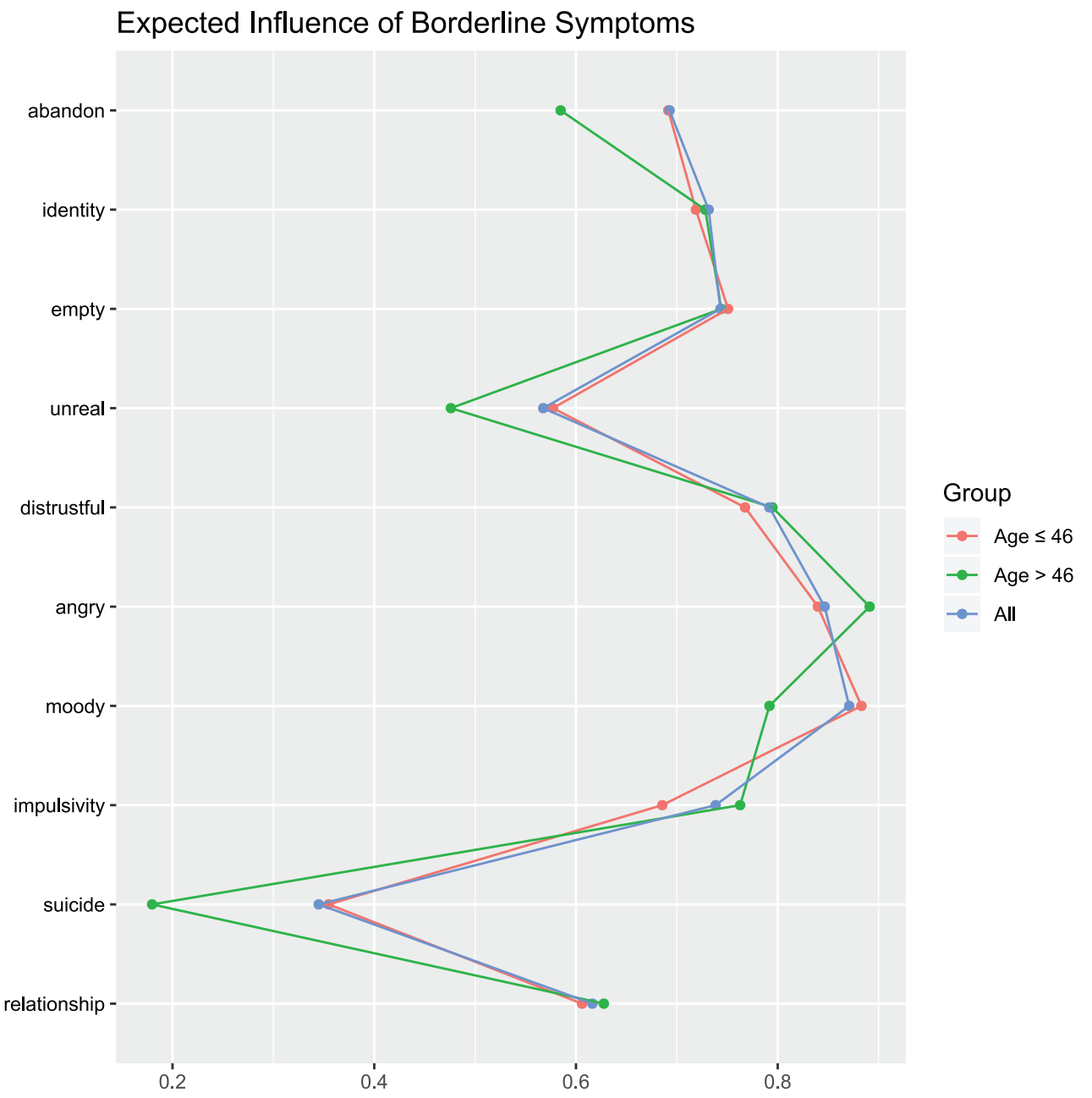

Fig. 2. Expected Influence of Borderline Symptoms. The y-axis lists each symptom from the 10 questions on the MSI-BPD measure, and the x-axis shows the expected influence centrality of each symptom. Higher centrality scores reflect greater relative importance of that symptom in the network.

individuals with BPD experience a relatively equivalent mix of both chronic and fluctuating symptoms (Conway et al., 2018), suggesting that the cross-sectional "snapshot" of symptoms in our data could be significantly influenced by situational increases in symptoms that precipitate partial hospitalization. The present study did not assess the onset or course of BPD symptoms, which further limits our ability to assess whether age-based differences are a result of developmental changes, situational stress, or a combination of these factors. Moreover, participants in this study were individuals across a broad age range seeking acute treatment for various psychiatric disorders, which further limits our ability to compare these results directly to those of longitudinal studies of individuals diagnosed with BPD. Longitudinal studies of BPD networks are an important next step; to our knowledge, no previous study has applied network analysis to evaluate changes in borderline symptom networks over time, or to test how borderline symptom networks may predict changes in the course of the disorder. Thus, future studies could apply these methods to longitudinal studies of BPD. However, cross-sectional networks have demonstrated some validity for clinical applications. Cross-sectional symptom and emotion network density (Pe et al., 2015; van Borkulo et al., 2015, but see also Schweren et al., 2018) and node centrality (Elliott et al., 2020; Olatunji et al., 2018; Rodebaugh et al., 2018) have been shown in some cases to predict clinical outcomes.

Despite the cross-sectional nature of these findings, the two network differences that emerged are consistent with previous research on age and symptoms. First, a large study of BPD highlighted that anger was one of the most persistent symptoms over a ten-year period of time (Zanarini et al., 2007). The role of anger in BPD is also a well-documented predictor of multiple functional consequences including aggression, treatment termination, and suicidality (Fernandez and Johnson, 2015). Beyond network differences, the high centrality of anger in symptom networks supports is consistent with evidence

showing the key role of enhancing control of anger during psychological treatment of BPD (e.g., Neacsiu et al., 2010). In parallel, we identified a weaker link between emptiness and NSSI/suicide attempts in the older group of participants. This finding is potentially consistent with prior research suggesting that NSSI is among the earliest symptoms to remit (Zanarini et al., 2007), although caution is warranted in interpreting this finding given that the cross-sectional design in the present study does not reveal if this weaker link is due to changes in emptiness or changes in NSSI.

In addition to the application of network analysis to longitudinal studies of BPD symptoms, future studies using network analysis for this population could also integrate measures assessing potential mechanisms of the disorder that may change with age. A number of studies have described mechanisms of psychopathology that show age-related variability, including sensitivity to facial affect (Rutter et al., 2019) and changes in cognitive control (Darowski et al., 2008). Each of these same mechanisms are implicated in BPD (Lynch et al., 2006; Ruocco, 2005); thus, future studies could integrate behavioral measures such as these into network analyses of BPD to evaluate their relationship with observed symptom changes. Finally, it should be noted that significant age-based differences were not present for a majority of symptom relationships. Future studies could potentially use Bayesian methods to assess the degree of network similarity between older and younger individuals (e.g., Williams et al., 2020).

Findings may also inform the selection of psychological treatment strategies for BPD symptoms. If the present study's findings of age-related differences in symptom relationships are replicated, future studies could investigate the utility of matching patients to appropriate treatment elements based on age. Moreover, the centrality of symptoms such as anger, affective instability (“extremely moody”), and distrust of others highlight the importance of addressing these symptoms in treatment. Indeed, several evidence-based treatments of BPD, such as Dialectical Behavior Therapy (DBT) or Transference-Focused Psychotherapy , explicitly focus on addressing these symptoms, with good efficacy (Levy et al., 2006; Neacsiu et al., 2010; Storbø et al., 2018). Beyond BPD, the centrality of these symptoms in the present transdiagnostic sample suggest that similar treatments may also yield similar benefits for individuals across the spectrum of psychopathology. This is consistent with the accumulating evidence for DBT as an efficacious treatment for transdiagnostic symptoms such as emotion dysregulation (Neacsiu et al., 2014; Ritschel et al., 2015).

Beyond the primary cross-sectional limitations described above, this study has several others that should be noted. First, our measure of BPD symptoms did not assess duration or severity of symptoms, which limits our ability to determine the proportion of participants meeting full criteria for BPD. Second, despite having good age representation, our sample was characterized by low ethnoracial diversity which limits the generalizability of findings. Finally, findings may be limited by the use of a relatively unique clinical sample (adults with heterogenous diagnoses seeking partial hospitalization), which may not generalize to symptoms of BPD more broadly.

In summary, this study supports the utility of network theory for elucidating potential age-related pathways by which symptoms of BPD change over time. Through the use of a novel machine learning method, we demonstrated that symptom networks significantly differ between older and younger adults, with a split point at age 46 maximizing heterogeneity between the two groups. If replicated using longitudinal methods, this finding suggests that treatments for BPD may benefit from being tailored to specific age-related groups of symptoms.

Contributors

A.D.P., P.J., and I.S. developed the study concept and design. A.D.P. and P.J. drafted the initial manuscript. P.J. performed the statistical analyses. I.S., I.W., C.B., and T.B. provided critical revisions. All authors have approved the final article.

Role of the funding source

The funding source had no involvement in the conduct of research or preparation of this article.

Declaration of Competing Interest

None.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2020.05.111.

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