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Original article

Depression–anxiety comorbidity network structure in Japanese and American midlife adults: A cross-cultural comparison using MIDUS and MIDJA

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ABSTRACT

Background: Cross-cultural comparisons of depression–anxiety comorbidity networks are limited. This cross-sectional study compared network structures between American and Japanese midlife adults (aged 30–79 years). Methods: Data were drawn from two harmonized datasets: the Midlife in the United States (MIDUS) 2 Biomarker Project ($N = 1230$) and the Midlife in Japan (MIDJA) 1 Biomarker Project ($N = 334$), its Japanese counterpart with parallel measures. We estimated comorbidity networks comprising 20 CES-D depression items and trait anxiety from the STAI using EBICglasso. The Network Comparison Test (NCT) was used to compare structure and global strength. A depression-only network comparison using CES-D items alone was also conducted. Results: No significant differences were observed in network structure or global strength, either in the full comorbidity networks or in the depression-only networks. Of four preregistered hypotheses, only Hypothesis 2 was supported: interpersonal symptoms showed higher centrality in the Japanese sample. Bridge centrality identified failure, enjoyment, happiness, and loneliness as primary symptoms connecting depression and anxiety. A notable cultural difference emerged in the fearful–anxiety connection, which was present in the American sample but absent in the Japanese sample. Bootstrap stability analysis indicated acceptable reliability for the MIDUS network. Limitations: The cross-sectional design precluded causal conclusions. The Japanese sample size limited statistical power and prevented reliable bootstrap analysis. Conclusions: These findings suggest similar depression–anxiety network architecture across cultures with meaningful symptom-level differences. Future longitudinal research with larger samples is needed to determine whether these patterns have implications for culturally adapted interventions.

1. Introduction

Depression and anxiety disorders are among the most prevalent mental health conditions worldwide. These two conditions frequently co-occur, sharing overlapping symptoms such as sleep disturbance, concentration difficulties, and fatigue, while also featuring distinct symptoms such as persistent sadness in depression and excessive worry in anxiety. Understanding the mechanisms underlying this comorbidity has important implications for its assessment, prevention, and treatment. The network approach to psychopathology offers a novel framework for examining comorbidity by conceptualizing symptoms as causally interconnected elements, rather than passive indicators of latent disease entities. This study applied network analysis to compare depression–anxiety comorbidity structures between Japanese and American midlife adults (defined as individuals aged 30–79 years), aiming to identify both universal and culturally specific patterns in how these disorders relate at the symptom level.

1.1. Depression–anxiety comorbidity: prevalence and clinical significance

The co-occurrence of depression and anxiety is one of the most robust findings in psychiatric epidemiology. A comprehensive meta-analysis by Saha et al. (2021), synthesizing 171 studies, found that all 90 pooled estimates for mood–anxiety comorbidity exceeded an odds ratio of 1.0, with a median odds ratio of 6.1. The comorbidity between depressive disorders and generalized anxiety disorder was particularly

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pronounced, with an adjusted odds ratio of 11.7. Data from the Netherlands Study of Depression and Anxiety (NESDA) revealed that among individuals with depressive disorders, 67 % had current comorbid anxiety and 75 % had lifetime comorbid anxiety (Lamers et al., 2011).

Comorbid depression and anxiety carry a substantially worse prognosis than either condition alone. The STAR*D study found that 53.2 % of outpatients with major depressive disorder met criteria for anxious depression, and these patients were significantly less likely to achieve remission, took longer to respond to treatment, and experienced greater side effect burden (Fava et al., 2008). Hirschfeld (2001) documented that comorbidity increases the risk of psychiatric hospitalization by 2.5-fold, while suicide attempts are 70 % higher when panic disorder accompanies depression. Given these clinical implications, understanding the mechanisms linking depression and anxiety at the symptom level is essential for developing more effective interventions.

1.2. The network approach to psychopathology

Traditional approaches to psychopathology have conceptualized mental disorders as latent disease entities that cause associated symptoms. The network approach offers an alternative perspective, proposing that mental disorders emerge from and are maintained by direct causal interactions among symptoms rather than by underlying latent conditions (Borsboom, 2017; Borsboom and Cramer, 2013). In this framework, symptoms are represented as nodes in a network, and statistical associations among symptoms are represented as edges connecting these nodes.

Cramer et al. (2010) applied network theory specifically to the problem of comorbidity, proposing that disorders co-occur because symptoms from different diagnostic categories directly activate one another. Rather than assuming that depression and anxiety share a common latent cause, the network perspective suggests that specific symptoms serve as bridges connecting the two domains. This reconceptualization has generated substantial research interest, with Robinaugh et al. (2020) identifying 363 network analysis articles published between 2008 and 2018, 60 % of which appeared in the final two years alone.

1.3. Bridge symptoms and comorbidity

Jones et al. (2021) formalized the concept of bridge centrality and introduced statistical indices to identify symptoms that connect different disorder clusters. Bridge symptoms are defined as those with strong connections to nodes in multiple communities (i.e., diagnostic categories); in the context of depression–anxiety comorbidity, these are symptoms that simultaneously connect to both depression and anxiety symptom clusters. Understanding bridge symptoms is clinically important because they may represent key intervention targets: if activation of one disorder spreads to another through specific bridge symptoms, targeting these symptoms could potentially prevent or reduce comorbidity. Simulation studies have demonstrated that deactivating bridge nodes is more effective in preventing comorbidity spread than targeting nodes with high traditional centrality, suggesting that bridge symptoms represent particularly important intervention targets (Jones et al., 2021).

Empirical studies have begun to identify the bridge symptoms in depression–anxiety networks. Kaiser et al. (2021), analyzing 5614 German inpatients with both major depressive disorder and anxiety disorders using the PHQ-9 and GAD-7, found psychomotor agitation/retardation, concentration problems, and restlessness to be the strongest bridge symptoms. Beard et al. (2016), examining 1029 partial hospital patients, found that sad mood and worry were among the most central symptoms in the depression–anxiety network. These findings suggest that specific symptoms may be particularly important for understanding and treating comorbid presentations, although the generalizability of these findings across cultural contexts remains unclear.

1.4. Cross-cultural perspectives on depression and anxiety

Cross-cultural research has documented meaningful differences in the experience and expression of depression and anxiety across various cultural contexts. Ryder et al. (2008), in a landmark comparison of Chinese and Euro-Canadian psychiatric outpatients, found that Chinese patients reported more somatic symptoms, whereas Euro-Canadian patients reported more psychological symptoms than their Chinese counterparts. Importantly, their analysis suggested that the Western emphasis on psychological symptoms may be as culturally specific as the East Asian emphasis on somatic symptoms. American cultural values emphasizing individual achievement, personal autonomy, and emotional expressiveness may shape how depression and anxiety manifest and interconnect in Western populations.

Research specific to the Japanese population has revealed distinctive patterns in mental health expression. Saint Arnault et al. (2006) found that female Japanese college students had significantly higher somatic distress scores than their American counterparts, with somatic distress explaining 31 % of the variance in depression scores for Japanese participants compared with only 1 % for Americans. The culture-specific syndrome of Taijin Kyofusho, characterized by fear of offending or embarrassing others rather than self-focused embarrassment, illustrates how anxiety manifests differently in Japanese cultural contexts (Essau et al., 2012). These cultural differences in symptom expression and conceptualization may produce different network structures, with implications for understanding comorbidity mechanisms across different cultures.

1.5. Cross-cultural network studies: a critical gap

Despite the rapid growth of network psychopathology research, cross-cultural applications are remarkably scarce. Robinaugh et al. (2020) explicitly noted the limitations of the generalizability of existing network findings across cultures. The few existing cross-cultural network studies have primarily focused on European samples or convenience populations. Fried et al. (2018) examined PTSD symptom networks across four trauma samples collected at European institutions and found moderate-to-high correlations for network structures and centrality estimates, supporting cross-cultural replicability within Western contexts. More recently, Mihić et al. (2024) conducted a cross-cultural network analysis of depression, anxiety, and stress symptoms across clinical samples from Serbia, Italy, and Croatia, finding a moderate degree of similarity across networks while identifying negative mood as the most central node. Noda et al. (2025) compared network structures of social anxiety, body dysmorphic, major depressive disorder, and shame symptoms among American, German, and Japanese populations, revealing significant cross-cultural differences between Japan and both Western samples (the United States and Germany) using the Network Comparison Test. However, no published study has compared depression–anxiety comorbidity networks between East Asian and Western populations using representative community samples to date.

This gap is particularly significant given that Japan and the United States exemplify contrasting cultural models—interdependent/collectivistic versus independent/individualistic self-construal (Markus and Kitayama, 1991)—which may systematically influence the relationship between depression and anxiety symptoms. However, it should be noted that the individualism-collectivism framework represents a simplified characterization of cultural differences; within-culture variability is substantial, and multiple cultural factors beyond self-construal (such as stigma, help-seeking patterns, and emotion regulation norms) may influence symptom networks. The availability of harmonized datasets from the Midlife in the United States (MIDUS) and Midlife in Japan

(MIDJA) studies provides a unique opportunity to address this gap using parallel measures in representative midlife samples.

1.6. The present study

The present study addresses the gap in cross-cultural network research by comparing depression–anxiety comorbidity network structures between American and Japanese midlife adults using data from the MIDUS 2 and MIDJA 1 Biomarker Projects. This study examined whether the overall network architecture and specific bridge symptoms differ between cultures, with implications for understanding both universal and culturally specific aspects of depression–anxiety comorbidity.

Based on the theoretical and empirical literature reviewed above, we tested the following hypotheses.

Hypothesis 1. (H1): Somatic symptoms will function as stronger bridges between depression and anxiety in the Japanese sample than in the American sample, consistent with documented patterns of somatic symptom emphasis in East Asian cultures.

Hypothesis 2. (H2): Interpersonal symptoms will show higher centrality in the Japanese sample than in the American sample, reflecting the greater importance of relational concerns in collectivistic cultural contexts.

Hypothesis 3. (H3): Optimal intervention targets (defined as high-centrality and high-bridge symptoms) will differ between cultures, such that network analysis will identify different priority symptoms for treatment in each cultural context.

Hypothesis 4. (H4): Positive affect items will show weaker bridge connections to anxiety in the Japanese sample than in the American sample, reflecting documented measurement non-invariance and cultural differences in positive emotion expression.

2. Methods

2.1. Transparency and open science statement

This study was preregistered on the Open Science Framework (OSF) prior to the data analysis (https://osf.io/wbu47/overview?view_only=b2ab28eb66c5456087b89d63e465f9cf). The preregistration specified the hypotheses, analytical approach, and the decision criteria. Data analysis was conducted according to a preregistered plan. We report how we determined our sample size, data exclusions, manipulations, and measures in this study.

2.2. Participants

2.2.1. United States sample

The American sample comprised participants from the MIDUS 2 Biomarker Project (ICPSR Study 29282) in the United States. The Midlife in the United States (MIDUS) is a national longitudinal study of health and well-being that began in 1995–1996 with a nationally representative sample of English-speaking adults aged 25–74 years, recruited via random digit dialing (Radler, 2014). MIDUS 2 (2004–2006) was the first follow-up, and the MIDUS 2 Biomarker Project (2004–2009) invited MIDUS 2 respondents to participate in an intensive two-day assessment at one of three General Clinical Research Centers (University of Wisconsin-Madison, Georgetown University, or UCLA). Participants completed self-administered questionnaires, physical examinations, and biological specimen collection. The detailed sampling procedure is described in Supplementary Material S1.

2.2.2. Japan sample

The Japanese sample comprised participants from the MIDJA 1 Biomarker Project (ICPSR Study 34969). MIDJA (Midlife in Japan) was designed as a Japanese companion study to MIDUS, with parallel survey instruments and biomarker protocols to enable direct cross-cultural comparison (Ryff et al., 2015). The MIDJA 1 Survey (2008) recruited 1027 adults aged 30–79 years through stratified probability sampling from the Basic Resident Register of the 23 special wards in the Tokyo metropolitan area. From this survey sample, a subsample was invited to participate in the Biomarker Project. The MIDJA 1 Biomarker Project (2009–2010) collected comparable biological and psychological data from respondents who completed an assessment at a clinic on the University of Tokyo campus in Japan. The detailed sampling procedure is described in Supplementary Material S1.

2.2.3. Analytic sample

The combined analytic sample included 1564 participants after listwise deletion of cases with missing data on any of the 20 CES-D items or the trait anxiety composite score: 1230 from the United States and 334 from Japan.

2.3. Measures

2.3.1. Center for epidemiologic studies depression scale (CES-D)

The CES-D (Radloff, 1977) is a 20-item self-report measure of depressive symptoms experienced in the previous week. Items are rated on a 4-point scale: 1 (rarely or none of the time), 2 (some of the time), 3 (much of the time), and 4 (most or all of the time). The scale comprises four subscales: Depressed Affect (seven items), Positive Affect (four items), Somatic Complaints (seven items), and Interpersonal Problems (two items). Internal consistency was good to excellent in both samples (MIDUS: McDonald's $\omega = 0.90$; MIDJA: McDonald's $\omega = 0.87$), computed using the psych package (Revelle, 2024). In the MIDUS 2 Biomarker Project, CES-D items were coded with variable names B4Q3A–B4Q3T. In the MIDJA 1 Biomarker Project, the corresponding variables were coded as J2Q43A–J2Q43T. Although the CES-D has been validated in Japanese populations (Shima et al., 1985), formal measurement invariance testing was not conducted in the present study; this limitation should be considered when interpreting cross-cultural comparisons.

2.3.2. Trait anxiety

Trait anxiety was assessed using the Trait Anxiety subscale of the State-Trait Anxiety Inventory (STAI; Spielberger et al., 1983). The trait anxiety subscale consists of 20 items that measure general tendencies to experience anxiety. Items are rated on a 4-point scale ranging from 1 (almost never) to 4 (almost always). A composite score was computed by summing all 20 items, with higher scores indicating greater anxiety. Internal consistency was excellent in both samples (MIDUS: Cronbach's $\alpha = 0.91$; MIDJA: Cronbach's $\alpha = 0.90$, as reported in the dataset documentation). McDonald's ω could not be computed for trait anxiety because the MIDUS and MIDJA Biomarker datasets provide only composite scores rather than individual item responses. In MIDUS, the composite variable is coded as B4QTA_AX, and in MIDJA, the corresponding variable is J2QTA_AX.

2.4. Data analysis

All analyses were conducted using R statistical software (version 4.5.2; R Core Team, 2025). Network estimation and analysis were performed using the qgraph (Epskamp et al., 2012), bootnet (Epskamp et al., 2018), and networktools (Jones et al., 2021) packages.

2.4.1. Network estimation

Depression–anxiety comorbidity networks were estimated separately for each sample using the EBICglasso algorithm (Extended Bayesian Information Criterion Graphical LASSO; Epskamp et al., 2018). This method estimates a Gaussian Graphical Model using LASSO

regularization with a tuning parameter selected to minimize the EBIC. Hyperparameter γ was set to 0.5, which provided a balance between sensitivity and specificity in edge detection. Polychoric correlations were computed using the cor_auto() function. Each network comprised 21 nodes: 20 CES-D items plus the trait anxiety composite score.

2.4.2. Centrality and bridge centrality analysis

Expected influence was used as the primary centrality metric, given the presence of both positive and negative edges. Bridge centrality was computed using the bridge function to identify symptoms connecting depression and anxiety domains. The nodes were assigned to two communities: CES-D items and trait anxiety. The bridge strength was calculated as the sum of the absolute edge weights connecting a node to nodes in the other community.

2.4.3. Bootstrap stability analysis

The stability of the centrality estimates was assessed using case-dropping bootstrap procedures with 1000 iterations (Epskamp et al., 2018). CS coefficients ≥ 0.50 were considered indicative of stable centrality estimates. Bootstrap analysis was conducted for the MIDUS sample ($N = 1230$). The MIDJA sample ($N = 334$) was insufficient for a reliable case-dropping bootstrap analysis with 21 network nodes.

2.4.4. Network comparison test

Network Comparison Tests (NCT; van Borkulo et al., 2023) with 1000 permutations were conducted to examine cross-cultural differences in the network structure and global strength. Three tests were performed: the network structure invariance test, global strength invariance test, and centrality difference test. The Bonferroni correction was applied for node-level comparisons (corrected threshold: $p < .0024$). In addition, to examine whether the depression symptom network alone differed between cultures, a separate network comparison was conducted using only the 20 CES-D items (without the trait anxiety composite). This depression-only analysis addressed the possibility that cross-cultural differences might be more apparent within a single symptom domain.

3. Results

3.1. Participants and descriptive statistics

The final analytical samples comprised 1230 American and 334 Japanese participants. Japanese participants reported significantly higher trait anxiety scores ($M = 39.51$, SD = 9.08) than American participants ($M = 34.27$, SD = 9.05). The CES-D total scores showed the opposite pattern, with Japanese participants reporting lower depression scores ($M = 29.63$) than American participants ($M = 35.26$). Trait anxiety and CES-D total scores were highly correlated in both samples (MIDUS: $r = 0.795$; MIDJA: $r = 0.775$).

3.2. Network estimation

Both networks showed comparable densities and maximum edge weights Fig. 1. The Japanese network exhibited greater global strength (12.70) than the American network (9.70), indicating stronger overall connectivity among depression and anxiety symptoms in the Japanese sample; however, this difference was not statistically significant (see Network Comparison Test results below).

A notable cross-cultural difference emerged in the fearful–anxiety connection: this edge was present in the American sample (0.114) but essentially absent in the Japanese sample (0.002). Conversely, the Enjoyed–Anxiety connection was substantially stronger in the Japanese sample (−0.191) than in the American sample (−0.050).

3.3. Preregistered hypothesis testing

Hypothesis 2, which predicted higher interpersonal symptom centrality in the Japanese sample, was supported. Interpersonal symptoms showed relatively higher centrality in the MIDJA sample (−0.0103) than in the MIDUS sample (−0.0933). Hypotheses 1 and 4 were not supported; contrary to predictions, somatic symptoms did not show stronger bridge centrality in the Japanese sample, and positive affect items showed stronger (not weaker) bridge connections in the Japanese sample. Hypothesis 3, predicting culturally specific intervention targets, was partially supported: while the overall network structure did not

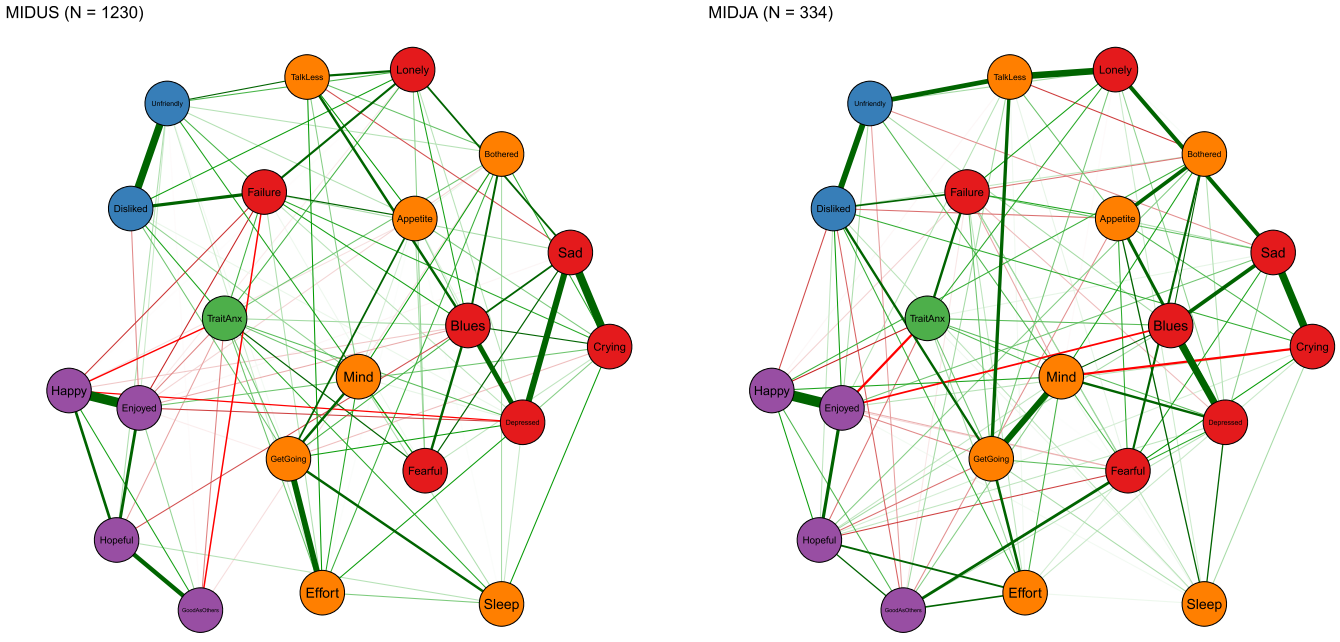

Fig. 1. Depression–anxiety comorbidity network structures for American (MIDUS; N = 1,230) and Japanese (MIDJA; N = 334) midlife adults. Nodes represent CES-D depression symptoms (20 items) and trait anxiety composite score. Blue edges indicate positive associations; red edges indicate negative associations. Edge thickness corresponds to regularized partial correlation strength. Networks were estimated using EBICglasso with γ = 0.5.

differ significantly, bridge symptom analysis revealed cultural differences in specific connections, particularly the fearful–anxiety connection.

3.4. Bootstrap stability analysis

The MIDUS centrality estimates demonstrated good to excellent stability (CS coefficients: Strength = 0.557 and Expected Influence = 0.750). The MIDJA sample was insufficient for a reliable bootstrap analysis.

3.5. Network comparison test

The NCT revealed no significant differences in the network structure ($M = 0.190$, $p = .382$) or global strength ($S = 3.006$, $p = .883$). Three nodes showed significant centrality differences at the uncorrected $\alpha = 0.05$ level: Mind ($p = .005$), Blues ($p = .007$), and Happy ($p = .050$). However, none survived the Bonferroni correction.

3.6. Depression-only network comparison

A separate network comparison using only the 20 CES-D items (without the trait anxiety composite) yielded results consistent with the full comorbidity network analysis. The CES-D-only networks showed comparable density (MIDUS: 0.647; MIDJA: 0.458) and global strength (MIDUS: 8.51; MIDJA: 8.01). The NCT for the depression-only networks revealed no significant differences in network structure ($M = 0.189$, $p = .422$) or global strength ($S = 0.505$, $p = .306$). No individual edges or centrality indices differed significantly after Bonferroni correction. These findings indicate that the structural similarity between the American and Japanese networks is not attributable to the inclusion of the trait anxiety composite score; rather, the depression symptom networks themselves are comparable across the two cultural contexts. An anxiety-only network comparison could not be conducted because the MIDUS and MIDJA Biomarker datasets provide only composite trait anxiety scores rather than individual STAI item responses Figs. 2 and 3.

4. Discussion

The present study examined the network structure of depression–anxiety comorbidity in American and Japanese midlife adults using data from the MIDUS and MIDJA Biomarker Projects. To our knowledge, this is the first study to compare depression–anxiety comorbidity networks between the United States and Japan using harmonized measurement tools.

4.1. Summary of findings

The Network Comparison Test revealed no significant differences in network structure ($M = 0.190$, $p = .382$) or global strength ($S = 3.006$, $p = .883$) between the samples. Of the four preregistered hypotheses, only Hypothesis 2 was supported; interpersonal symptoms showed relatively higher centrality in the Japanese sample. Bridge centrality analyses identified failure, enjoyment, happiness, and loneliness as the primary symptoms connecting the depression and anxiety domains.

4.2. Network similarity across cultures

The finding that depression–anxiety comorbidity networks did not significantly differ in terms of overall structure or strength has important theoretical implications, though these null findings must be interpreted cautiously. Network theory conceptualizes mental disorders as systems with causally interacting symptoms (Borsboom, 2017). One interpretation of the absence of significant structural differences is that fundamental mechanisms linking depression and anxiety may operate similarly across different cultural contexts. This pattern is consistent with that of Fried et al. (2018), who found moderate-to-high correlations in PTSD network structures across European samples. Notably, the depression-only network comparison using 20 CES-D items without the trait anxiety composite yielded the same pattern of non-significant differences in both network structure and global strength, suggesting that this similarity is not an artifact of including the composite trait anxiety score. However, an alternative explanation is that the relatively small Japanese sample ($N = 334$) may have provided insufficient statistical power to detect genuine cross-cultural differences. Network comparison tests with 21 nodes typically require larger samples for adequate power, and the instability of the Japanese network (which precluded reliable bootstrap analysis) suggests that any subtle cross-cultural differences may have been obscured by estimation uncertainty. Therefore, the null findings regarding overall network structure should not be interpreted as definitive evidence of structural equivalence.

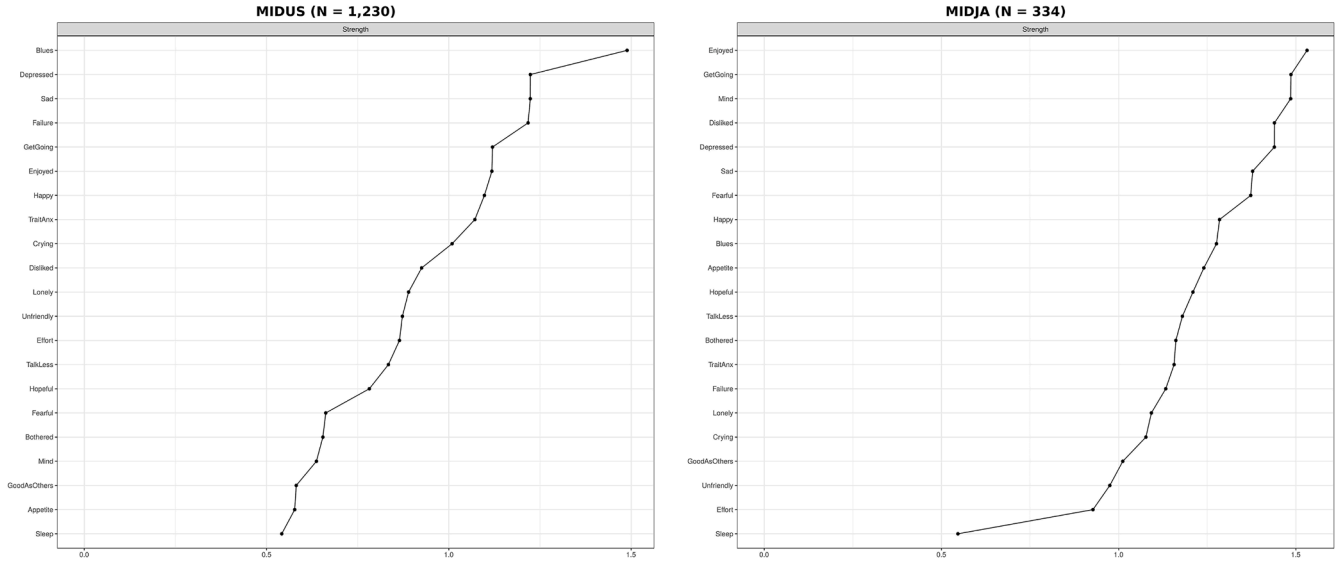

Fig. 2. Node strength centrality comparison between MIDUS and MIDJA samples. Bars represent standardized strength centrality values for each symptom. Symptoms are ordered by centrality in the MIDUS sample. Blues and Depressed showed the highest centrality in both samples.

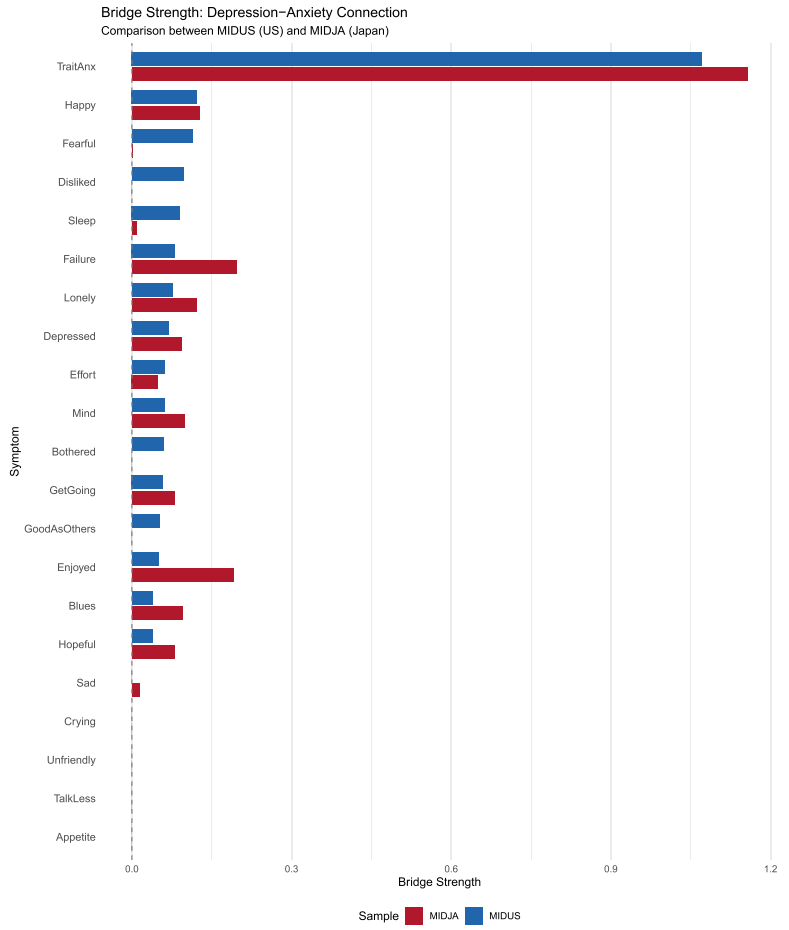

Fig. 3. Bridge strength centrality comparison between MIDUS (United States) and MIDJA (Japan) samples. Bridge strength quantifies the extent to which each symptom connects depression and anxiety domains. TraitAnx (trait anxiety), Happy, Fearful, Disliked, and Sleep showed the highest bridge strength values. Notable cultural differences emerged in the Fearful–TraitAnx connection.

4.3. Bridge symptoms connecting depression and anxiety

The identification of failure, enjoyment, happiness, and loneliness as primary bridge symptoms has implications for understanding comorbidity mechanisms. Jones et al. (2021) proposed that bridging symptoms may explain the frequent co-occurrence of disorders. The present findings suggest that worthlessness, anhedonia, and social disconnection may be particularly important in linking depression and anxiety symptoms.

Prior research on depression–anxiety bridge symptoms has yielded somewhat different findings, likely reflecting differences in the measurement instruments. Kaiser et al. (2021), analyzing 5614 German inpatients using the PHQ-9 and GAD-7, found psychomotor agitation/retardation, concentration problems, and restlessness to be the strongest bridge symptoms. Beard et al. (2016) found that sad mood and worry were among the most central symptoms in a sample of partial hospital patients. The present study's use of the CES-D, which includes distinct items for positive affect and interpersonal symptoms, may account for the prominence of affective and social symptoms as bridges in our study.

4.4. Cultural differences in the fearful–anxiety connection

Perhaps the most striking cross-cultural difference was the presence of the fearful–anxiety connection in the American sample but its virtual absence in the Japanese sample. This finding warrants careful interpretation given the cross-sectional design. Cross-cultural emotion research has documented that Japanese individuals recognize a substantial difference between kyofu (fear) and fuan (anxiety), with fuan being experientially closer to depression than to fear (Saint Arnault et al., 2005). The culture-specific syndrome of Taijin Kyofusho demonstrates how anxiety in Japanese contexts is oriented toward interpersonal rather than intrapersonal concerns (Essau et al., 2012). The absence of the fearful–anxiety connection in the Japanese network may reflect these linguistic and conceptual distinctions: if Japanese respondents interpret the "fearful" item as referencing kyofu (specific fear) rather than fuan (general anxiety), this would weaken its association with trait anxiety. However, this interpretation remains speculative without direct examination of item-level response patterns and qualitative data on how participants understood these items.

4.5. Higher interpersonal symptom centrality in Japan

The supported hypothesis regarding higher interpersonal symptom centrality in the Japanese sample aligns with research on self-construal. Markus and Kitayama (1991) distinguished between independent and interdependent self-construal, proposing that individuals in collectivistic cultures define themselves through relationships with others. The higher centrality of interpersonal symptoms in the Japanese network is consistent with the cultural emphasis on social harmony and suggests that relational concerns may play a more prominent role in the depression–anxiety system for Japanese individuals. From a network perspective, higher centrality indicates that interpersonal symptoms have stronger and more numerous connections to other symptoms in the network. This could mean that in Japanese cultural contexts, disruptions in interpersonal relationships may have more widespread effects on

other depression and anxiety symptoms. However, as noted earlier, centrality in cross-sectional networks does not establish causal importance, and this interpretation remains tentative pending longitudinal investigation.

4.6. Clinical implications

The identification of failure, enjoyment, happiness, and loneliness as bridge symptoms provides preliminary hypotheses about which symptoms might link depression and anxiety. However, several important caveats must be noted. First, centrality in a cross-sectional network does not imply causal importance; high centrality indicates statistical association strength, not that a symptom causes or maintains comorbidity. Rodebaugh et al. (2018) found limited evidence that cross-sectional centrality predicts treatment outcomes, noting that centrality indices showed no ability to identify symptoms influencing measures beyond the modeled network, highlighting the uncertain relationship between network position and clinical significance. Second, the cross-sectional nature of this study precludes any causal inferences about symptom relationships. Third, for the Japanese population, while higher interpersonal centrality is consistent with theoretical predictions about collectivistic cultures, this finding requires replication with larger samples before informing clinical practice. Therefore, the present findings should be viewed as generating hypotheses for future longitudinal research rather than providing direct guidance for clinical interventions.

4.7. Limitations

This study has several limitations that warrant careful consideration. First and most critically, the Japanese sample ($N = 334$) was insufficient for reliable bootstrap analysis with 21 nodes, and this limited sample size raises concerns about statistical power for detecting cross-cultural differences. The null findings regarding overall network structure may therefore reflect Type II error rather than true structural equivalence. Second, formal measurement invariance testing was not conducted; without establishing that the CES-D and STAI function equivalently across cultures, observed differences (or lack thereof) may partially reflect measurement artifacts rather than true psychological differences. Third, the cross-sectional design precludes causal conclusions from being drawn; network edges represent statistical associations, not causal relationships. Fourth, the study used a single trait anxiety composite rather than individual anxiety items, which limited our ability to examine specific anxiety symptoms; the MIDUS and MIDJA Biomarker datasets do not provide individual STAI item responses, which precluded both an anxiety-only network comparison parallel to the depression-only analysis and the computation of McDonald's ω for this measure. Fifth, the CES-D was developed within the Western framework, potentially introducing cultural bias. Sixth, mental health stigma in Japan (Ando et al., 2013) and low rates of mental health service utilization (Naganuma et al., 2006) may affect symptom reporting. Finally, the samples were recruited from specific geographical regions (Tokyo metropolitan area for Japan; multiple sites in the US), which may limit generalizability.

4.8. Conclusions

This study provides the first comparison of depression–anxiety comorbidity networks between American and Japanese midlife adults using harmonized measures. Despite cultural differences in mean symptom levels, the overall network structure and global strength did not differ significantly, although limited statistical power precludes definitive conclusions about structural equivalence. Meaningful cultural differences emerged at the symptom level, including higher interpersonal symptom centrality in Japan and the absence of a fearful–anxiety connection in the Japanese sample. These cross-sectional findings contribute to the understanding of both universal and culturally specific aspects of depression–anxiety comorbidity. However, given the limitations of cross-sectional network analysis—particularly that centrality does not imply causal importance—these findings should primarily inform future longitudinal research rather than immediate clinical application. Larger-scale studies with formal measurement invariance testing are needed to confirm these patterns and determine their clinical relevance for culturally adapted interventions.

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Data availability

The data used in this study are publicly available from the Inter-university Consortium for Political and Social Research (ICPSR). The MIDUS 2 Biomarker Project data are available at https://doi.org/10.3886/ICPSR29282.v10 (ICPSR Study 29282). The MIDJA 1 Biomarker Project data are available at https://doi.org/10.3886/ICPSR34969.v4 (ICPSR Study 34969). The analysis code is available from the corresponding author upon reasonable request.

Ethics statement

This study represents a secondary analysis of de-identified publicly available data from the Midlife in the United States (MIDUS) and Midlife in Japan (MIDJA) studies. The original MIDUS Biomarker Project received approval from the Institutional Review Boards at the University of Wisconsin-Madison, Georgetown University, and UCLA. The original MIDJA Biomarker Project was approved by the ethics committees of the University of Tokyo and Nihon University. All procedures performed in the original studies involving human participants were in accordance with the ethical standards of the institutional and national research committees and with the 1964 Helsinki Declaration and its later amendments. Informed consent was obtained from all individual participants included in the original studies. This secondary analysis used de-identified data obtained from the Inter-university Consortium for Political and Social Research (ICPSR) under data use agreements.

Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this manuscript, the authors used Paperpal in order to improve language and readability. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

CRediT authorship contribution statement

Takayuki Fujii: Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Taiga Seo:** Writing – review & editing. **Yuji Nogami:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

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