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The structure of depressive symptoms using CES-D and ZDS in outpatients in a general hospital in Lima, Peru



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ABSTRACT

Background: Depression represents one of the leading causes of disability due to illness worldwide. Previous studies have demonstrated the significant heterogeneity of the diagnosis of depression, making it necessary to develop new diagnostic approaches. Network analysis is a perspective that considers symptoms as constituents of the psychiatric disorder itself. The objective was to determine the structure of depressive symptoms using the CES-D and ZDS depression scales.

Methods: Cross-sectional study of secondary analysis of 194 patients using the CES-D and ZDS scales. Correlation matrices and regularised partial correlation networks were constructed from the database. Centrality measures were estimated, and a network stability analysis was performed.

Results: On the CES-D scale, the most central item was “Sad”; while on the ZDS scale, the most central items were “Sad” and “Live”. On the CES-D scale, the connection between “Enjoy” and “Happy” was the strongest. On the ZDS scale, the strongest connection was between the items “Live” with “Useful”. The item “Morning” was the least connected on the ZDS.

Conclusions: The most central symptom from the CES-D scale was sadness, while from the ZDS scale, was sadness and anhedonia.

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Estructura de los síntomas de depresión según el CES-D y la ZDS en pacientes ambulatorios de un hospital general de Lima, Perú

R E S U M E N

Palabras clave:

Depresión

Psicopatología

Síntomas afectivos

Introducción: La depresión es una de las principales causas de discapacidad por enfermedad en el mundo. Estudios previos han demostrado la gran heterogeneidad del diagnóstico de depresión, por lo que es necesario desarrollar nuevas aproximaciones diagnósticas. El análisis de redes es una perspectiva que considera los síntomas como constituyentes del trastorno psiquiátrico. El objetivo es determinar la estructura de síntomas depresivos a partir de las escalas para depresión CES-D y ZDS.

Métodos: Estudio transversal de análisis secundario de 194 pacientes mediante las escalas CES-D y ZDS. A partir de la base de datos se elaboraron matrices de correlaciones y redes de correlaciones parciales regularizadas, se estimaron medidas de centralidad y se realizó un análisis de estabilidad de la red.

Resultados: En la escala CES-D, el ítem más central fue «Triste», mientras que en la escala ZDS lo fueron «Triste» y «Vivir». En la escala CES-D, la conexión entre «Disfrutar» y «Contento» fue la más fuerte. En la escala ZDS, fue entre los ítems «Vivir» y «Útil». El ítem «Mañanas» fue el menos conectado de la red ZDS.

Conclusiones: El síntoma más central de la escala CES-D fue la tristeza, mientras que en la ZDS fueron la tristeza y la anhedonia.

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Introduction

Depression is a psychiatric disorder that affects many people all over the world. According to the WHO, approximately 350 million worldwide suffer from depression and it is the leading cause of years lost due to disability; 76.4 million years, equivalent to 10.3% of the total burden of diseases. In Peru, the prevalence in 2010 was 4.89% (95% confidence interval [95%CI], 3.36%–7.06%).¹

Depression, considered as a syndrome, is a heterogeneous group of symptoms which gives rise to a variable presentation depending on the onset, severity, course of the disease and the particular set of symptoms. According to the fifth edition of the *Diagnostic Statistical Manual of Mental Disorders* (DSM-5), major depression is characterised by the presence of at least five symptoms from a list of nine, which must include sadness or anhedonia.² The permutation of these nine symptoms leads to a wide variety of possible forms of presentation.

A study of 3703 patients diagnosed with depression analysed the variation in depressive symptoms in each clinical condition and found a total of 1030 possible patterns. The most common pattern in that study had a frequency of 1.78%, which shows great heterogeneity in the presentation of depression and calls into question the consistency of the diagnosis.³

In current disease classification systems, such as the DSM-5, it is considered that the symptoms and signs that patients report have their origin in a latent cause called a mental disorder, and that these are grouped together, forming discrete entities with clear boundaries between them.⁴

In psychiatry, we talk about mental disorders, not illnesses, as occurs in other branches of medicine, because illnesses arise from a common pathogenic pathway, while

mental disorders are syndromic constellations of empirically linked symptoms. A syndrome consists of multiple inter-related symptoms with a stable and characteristic structure, as well as a particular prognosis.⁵

Therefore, if a syndrome corresponds to a natural entity, there should be some natural limit or discontinuity between mental disorders. The problem with this perspective, which conceives mental disorders as distinct categories, is explaining the high comorbidity of mental disorders or the almost non-existent presence of pathognomonic symptoms.^{5,6}

Conceiving mental disorders as a common cause underlying the set of symptoms (syndrome) has not been so effective, as it has not been possible to identify any pathogenic pathway or aetiological mechanism for these mental disorders.⁵

From this theoretical model that understands mental disorders as unknown causes of observable symptoms, statistical models have been developed, such as the latent variable model, in which the symptoms are observable variables of a mental disorder (latent variable). One example of these models is factor analysis, often used in the development of psychometric scales.⁶

The network approach proposes that mental disorders are not underlying causes of observable symptoms but rather interconnected symptoms which interact.⁶ This theoretical approach to mental disorders requires a statistical method that allows models to be developed related to the proposed theoretical framework: network analysis.

This seeks to complement the limitations of the latent variable model. This approach arises from the following statements: (a) current information does not let us explain the concomitance of symptoms of a certain disorder based on a specific biological or psychological condition; and (b) in psychopathology, the symptoms can be causally related to each

other.⁷ This means that an underlying disorder would not be the common cause of the covariance between symptoms, but rather the interaction between symptoms would be constitutive of the disorder.⁴

The networks are drawn up from correlation matrices of symptoms and made up of nodes, which represent the symptoms, and edges, which represent their association. Edges can, in turn, be weighted or unweighted and directed or undirected. Weighted edges are distinguished from unweighted edges because they quantify the magnitude of the connection between symptoms. The directionality indicates a possible causal relationship between items. The edges can represent positive or negative associations of symptoms and appear as different colours (usually green for positive relationships and red for negative relationships).⁸

Central symptoms represent an important concept within network analysis. These are assessed using measures of centrality (for example, strength, closeness or intermediation) which describe degrees of connectivity of a symptom with others in magnitude and quantity. Due to these characteristics, central symptoms allow both the activation and maintenance of the network in the disease state. The strong connectivity of these symptoms within the network would make them a target for more effective biological or psychosocial interventions.⁷

Furthermore, the central symptoms of the same disorder could vary depending on the group to which the network analysis is applied. Thus, symptoms such as the desire for death, depressed mood, loss of interest and pessimism constitute the basis of depressive symptoms in old age,⁹ while in women with postpartum depression, it would be caused by fatigue, sadness and anhedonia.¹⁰ In a network analysis study carried out on psychiatric outpatient patients, a structure of depressive symptoms was identified consisting of sadness, loneliness, vulnerability, ideas of death, guilt and worthlessness, and the first three were the most important.¹¹

Among the limitations of this type of study are its small sample size and reproducibility. Even though the number of investigations supporting the reproducibility of results in different samples is large, the cross-sectional nature does not allow us to determine causality between the symptoms.¹² This study seeks to evaluate a clinical population from the Psychiatry and Internal Medicine clinic of a general hospital and thus assess the reproducibility of the structure found in previous studies on the general population based on the Center for Epidemiologic Studies Depression Scale (CES-D) and the Zung Self-Rating Depression Scale (ZDS).

Both are consistent instruments for the detection of depressive symptoms in a hospital environment and in the general population, and could be an important contribution to both research and diagnosis of major depressive disorder. It is important to improve the understanding of depressive psychopathology and its symptoms, given the frequency of underdiagnosis of depressive disorders in primary care in developing countries¹³ and the still deficient prevention, treatment and rehabilitation of depressive disorders in Latin America.¹⁴

Our study contributes this evidence to the instruments used in Spanish and Spanish-speaking countries, which has been limited until now. The results obtained will enable us

to determine the symptom structure of the depressive disorder, visualise this structure and identify the central symptoms according to the CES-D and ZDS.

Methods

This was a cross-sectional secondary data analysis study. We decided to perform a secondary analysis due to the current limitations in data collection caused by the COVID-19 pandemic. We used the database of a study carried out by Ruiz-Grosso et al.,¹⁵ aimed at validating and comparing the psychometric properties of the Spanish versions of the CES-D¹⁶ and ZDS.¹⁷ In network analysis, the use of databases from psychometric studies that contain items representative of multiple dimensions of the disorder under evaluation is common. To this extent, the database used has the advantage of including two instruments validated in Spanish with adequate psychometric properties. Furthermore, as it included a clinical population not restricted only to patients with a diagnosis of major depression, it avoided conditioning the variables on a certain scale score.

The study was carried out at the Hospital Cayetano Heredia (Lima, Peru) from January to December 2006. The study had the informed consent of the participants and the authorisation of the Ethics Committee of the Hospital Cayetano Heredia and the Universidad Peruana Cayetano Heredia.

A total of 194 records from the aforementioned validation study¹⁵ were used. These records came from patients in the Psychiatry and Internal Medicine outpatient clinic and included 70 patients with a diagnosis of major depression (MD), 63 with a psychiatric disorder other than major depression (OP), and 61 without evidence of a psychiatric disorder (NP). The inclusion criterion in the MD subgroup was the diagnosis of major depression made by a psychiatrist using DSM-IV criteria. The inclusion criterion in the OP subgroup consisted of a diagnosis of other psychiatric disorders (including bipolar disorder) by a psychiatrist using DSM-IV criteria.

There is no consensus to determine the sample size in network analysis. A sample size of 194 has been considered acceptable following the recommendations established for factor analysis studies.¹⁸ Simulation studies show that a 20-node network with 200 participants would have a sensitivity around 0.8 and a specificity around 0.9.¹⁹ The adequacy of the sample size was confirmed after obtaining results through stability analysis.²⁰

Tools

The Center for Epidemiologic Studies-Depression Scale (CES-D) in its Spanish version has 20 Likert-type items and was designed to detect depressive disorders in the general population. Each item on the scale scores from 0 to 3. It has good internal consistency (Cronbach's alpha, 0.93).¹⁶

The Zung Self-rating Depression Scale (ZDS) in its Spanish version is a 20-item Likert-type scale that enables depressive symptoms to be identified at the first level of care. Each item on this scale scores from 1 to 4. It has good internal consistency ($\alpha = 0.89$).¹⁷

Statistical analysis

R version 4.03 was used for the statistical analysis using the integrated development environment RStudio version 1.4.1103. The database of the original extension study *.dta was imported into RStudio.

Correlation matrices were generated that estimate the association between variables assumed to be continuous but measured on an ordinal scale. The *cor.auto* function of the *qgraph* software, version 1.6.9 was used, which automatically attributes the best correlation method for Likert-type ordinal variables.^{7,21}

A regularised partial correlation network was estimated based on the correlation matrix. The network was built with the *estimate Network* function from the *bootnet* package. When considering partial correlations, the connections between nodes represent relationships of conditional independence between nodes, and each relationship between a pair of nodes is given by controlling the effect of the other nodes. The network estimation was carried out using the EBIC-glasso model, which includes the regularisation technique, glasso (Graphical Least Absolute Shrinkage and Selection Operator) and EBIC (Extended Bayesian Information Criterion). The glasso algorithm is a regularisation method that allows the connections in the network to be reduced by setting the smallest connections to 0. This helped eliminate spurious relationships and maintain a more dispersed and parsimonious network.²²⁻²⁴ The EBIC method is a selection criterion that estimates 100 network models with different degrees of dispersion and selects the one with the lowest EBIC according to the hyper-parameter γ , which regulates the balance between the inclusion of false positives and the removal of true connections. We chose an intermediate value of $\gamma=0.5$.²²

The Fruchterman-Reingold algorithm was used to design the network, based on strength, which places the most interconnected symptoms towards the centre of the network and prioritises the visual appearance of the network.^{24,25}

Centrality measures allow us to know which items have a greater number of connections with other items, as well as stronger connections. Only the strength centrality measure was calculated using the *qgraph centrality.auto*.^{20,21,24,25}

An *a posteriori* stability analysis was carried out, which determines the correlation stability coefficient using the bootnet function of the R bootnet statistical package. This analysis allows the stability of the centrality measures of each network to be established by randomly reducing the sample size with respect to the original sample.²¹

Ethical considerations

For this study, we used a database of 194 records from a 2006 study at Hospital Cayetano Heredia, which had authorisation from the hospital's Ethics Committee and the Universidad Peruana Cayetano Heredia. This database does not allow participants to be identified, so it was not possible to obtain new informed consent, but it caused them no harm. This study's protocol is registered in the Sistema Descentralizado de Información y Seguimiento a la Investigación (SIDISI) [Decentralized Research Information and Monitoring System] and was exempt from review by the Comité Institucional de Ética en Investigación [Institutional Research Ethics Committee] de la Universidad Peruana Cayetano Heredia (CIEI-UPCH).

Results

Regularised partial correlation network

Fig. 1 shows the regularised partial correlation network obtained from the CES-D. The network in general is positively connected and the connections show the different degrees of correlation between the variables. The item pairs with the highest correlation are "I enjoyed life" and "I was happy" ($r=0.37$) and "I felt that I could not shake off the blues even with help from my family or friends" and "I felt depressed" ($r=0.27$). In the network, only one negative correlation was found between the items "I felt that I was just as good as other people" and "I felt that everything I did was an effort" ($r=-0.07$).

Fig. 2 shows the regularised partial correlation network obtained from the ZDS. The network in general is positively connected and the items with the highest correlation are: "I feel downhearted and blue" and "I have crying spells or

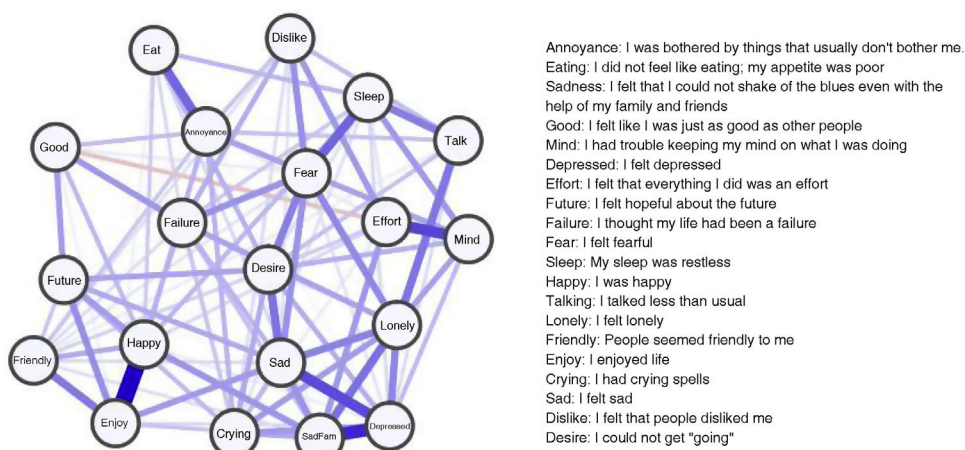


Fig. 1 – Network of partial correlations regularised from the CES-D using the EBICglasso algorithm.

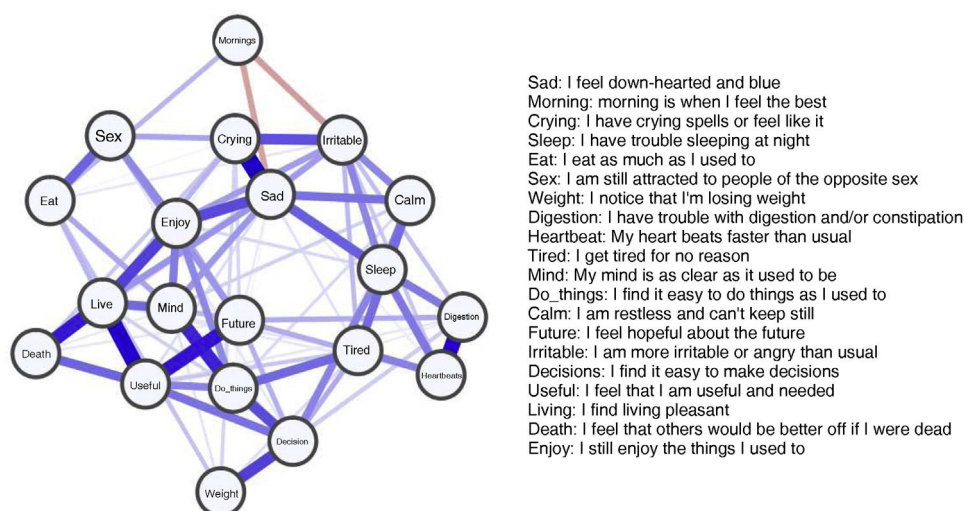


Fig. 2 – Network of partial correlations regularised from the ZDS using the EBICglasso algorithm.

feel like it" ($r=0.31$), "I find living pleasant" and "I feel useful and needed" ($r=0.28$). Two negative correlations were found between "In the mornings I feel better about my sadness" and the items "I feel downhearted and blue" ($r=-0.1$) and "I am more irritable or angry than before" ($r=-0.1$).

Centrality measures

Figs. 3 and 4 show the centrality graphs of the two scales. Centrality measures indicate the relative importance of a node within the network, as well as its influence on the activation of other nodes. On the CES-D scale, the item with the highest centrality strength is "I felt sad" ($Z=1.63$), while in the ZDS it is "I feel downhearted and blue" ($Z=1.92$), followed by "I find living pleasant" ($Z=1.73$). The least central item on the CES-D scale is "I felt that I was just as good as other people" and on the ZDS, "In the mornings, I feel better about my sadness."

Stability of the network

To evaluate the stability of the network, a bootstrap case-dropping analysis was carried out in which the sample size is randomly reduced, and the centrality measures of the networks with a reduced sample are correlated with the centrality measures of the original network. Fig. 5 shows that the network obtained from the CES-D scale allows a maximum reduction of up to 36.1% in the sample size to maintain a centrality correlation with the original sample of 0.7 with a 95%CI. Fig. 6 shows that the network obtained from the ZDS scale allows a maximum reduction of up to 20.6% to maintain a centrality correlation with the original sample of 0.7.

Discussion

In this study, a network analysis of partial correlations was performed for each scale (CES-D and ZDS). Both the network graph of the ZDS scale and that of the CES-D scale (Figs. 1 and 2) are positively connected, and the graph of the ZDS scale is

more dispersed, that is, with fewer connections. This could be because the CES-D has items that assess the same construct, as in the case of "I felt sad", "I felt depressed" and "I felt that I could not shake off the blues even with help from my family and friends", which evaluate negative mood.²⁶

In weighted indirect networks, such as those shown (Figs. 1 and 2), connections can be interpreted as simple paired associations, as potential pathways of causality or as predictors. If you have the A-B connection, the following interpretations can be generated: A is associated with B; it is possible that $A \rightarrow B$, $A \leftarrow B$ or that $A \leftarrow C \rightarrow B$ or that A predicts B or vice versa.

In the network graph of the CES-D scale (Fig. 1), the strongest connection, without considering those that assess the same construct, was between "I felt that everything I did was an effort" and "I had trouble keeping my mind on what I was doing".

For the sample evaluated and controlling the effect of the other nodes, this connection can be interpreted as a strong association between difficulties in carrying out tasks and concentration problems. Problems with concentration can cause difficulty in completing tasks, or difficulties in completing tasks can cause problems with concentration, or the occurrence of problems with concentration can predict difficulties in completing tasks or vice versa.

Another of the strongest connections found in the network of the CES-D scale (Fig. 1) is between the items "I felt sad" and "I felt lonely". This connection can be interpreted as there being a strong association between sadness and loneliness; sadness can cause feelings of loneliness; the feeling of loneliness can cause sadness, or the feeling of loneliness can predict sadness or vice versa.

If these findings are transferred to the clinical setting of a patient with depression, it could be pointed out that intervening to improve the ability to concentrate could lead to requiring less effort for activities, and that intervention in social habits would contribute to improving the mood, which is consistent with the results of cognitive remediation interventions.²⁷

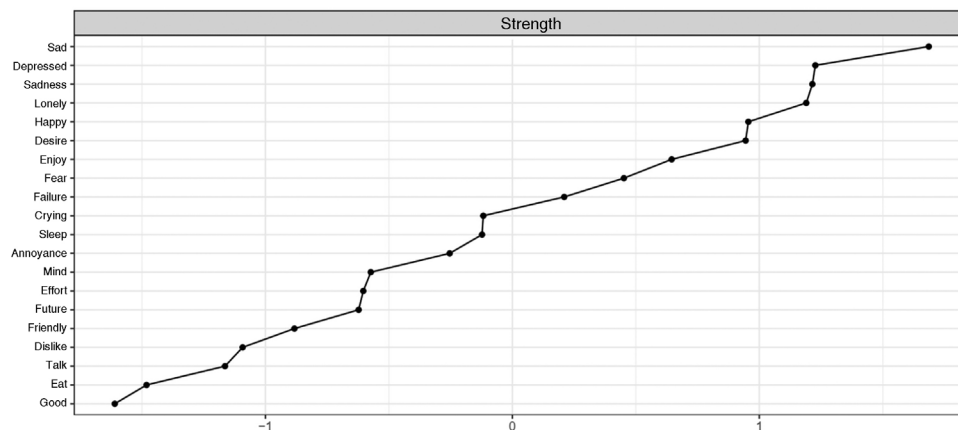


Fig. 3 – Centrality (strength) graph of the CES-D in Z-score.

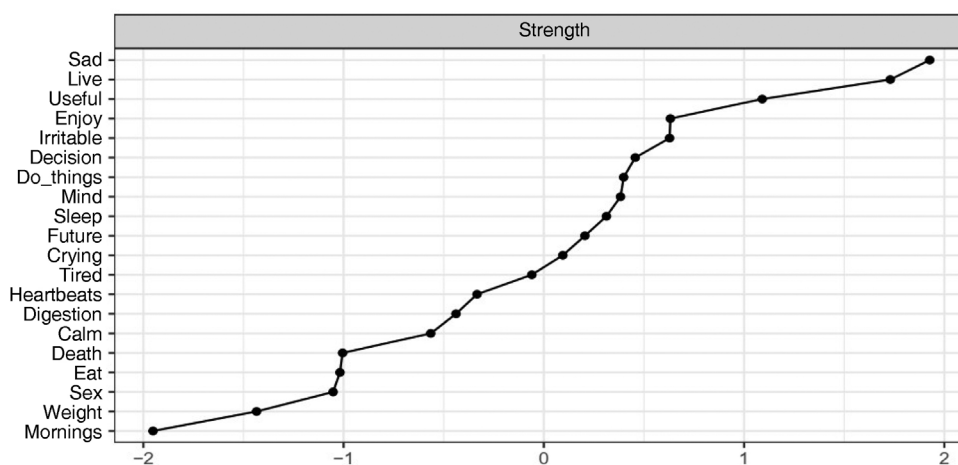


Fig. 4 – Centrality (strength) graph of the ZDS in Z-score.

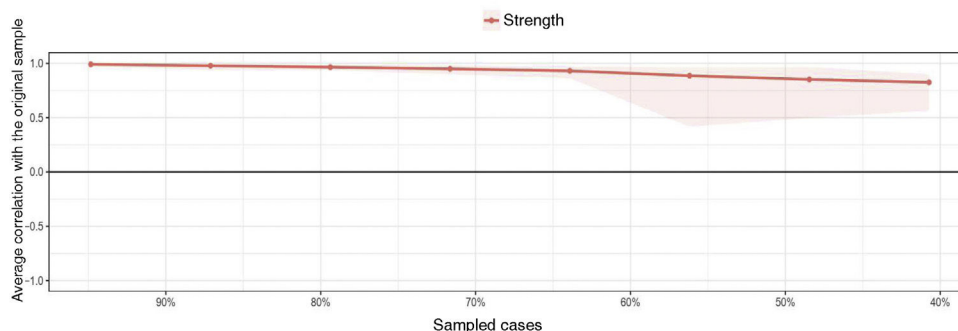


Fig. 5 – Stability graph of the network constructed from the CES-D (95%CI).

Previous network analysis studies with the CES-D also showed a strong connection between the items “I felt sad” and “I felt lonely”, such as the study by Santos et al.²⁸ in pregnant women between 22 and 24 weeks, and the study by Burger et al.²⁹ in people going through the loss of a partner due to separation or death. Furthermore, the distribution of symptoms in the network groups the symptoms in accordance with factor analysis studies of the CES-D scale, and coincides in the anhedonia factor (items “I felt that I was just as good as other people”, “I felt optimistic about the future”, “I was happy” and

“I enjoyed life”) and the negative affect factor (items “I felt that I could not shake off the blues even with help from my family and friends”, “I felt depressed”, “I felt lonely” and “I felt sad”).³⁰

In the network graph of the ZDS scale (Fig. 2), the strongest connections, without considering those that assess the same construct, are between “I feel useful and needed” and “I find living pleasant”.

For the sample assessed and controlling the effect of the other nodes, this connection can be interpreted as there being a strong association between the feeling of worthlessness and

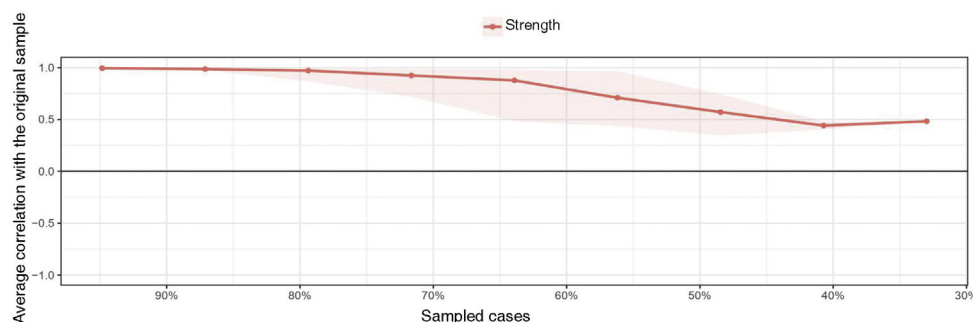


Fig. 6 – Stability graph of the network constructed from the ZDS (95%CI).

anhedonia; feeling worthless can lead to not enjoying life, or finding life unpleasant can cause a feeling of worthlessness, or having a feeling of worthlessness can predict anhedonia or vice versa.

Another of the strongest connections found in the CES-D network (Fig. 1) is between the items “I feel useful and needed” and “I felt hopeful about the future”. This connection can be interpreted as a strong association between the feeling of worthlessness and hopelessness; feeling worthless can lead to losing hope in the future, or not having hope in the future can cause feelings of worthlessness, or feeling worthless can predict hopelessness or vice versa.

If these findings are transferred to the clinical setting of a patient with depression, it could be pointed out that intervening to make a patient feel more useful could make them enjoy their activities more and give them a more optimistic vision about the future, which coincides with the results of behavioural activation interventions.³¹

The items “I have trouble with digestion and/or constipation” and “My heart beats faster than usual” also have a strong connection as somatic symptoms, which could be explained by the fact that they respond to a common autonomic pathway, and they are also symptoms of the anxiety spectrum in the DSM-III.³² These results are in line with other network analysis studies and the depression-anxiety continuum hypothesis.^{33,34}

The centrality of the items was evaluated based on the centrality (*strength*) measure, which denotes the weighted sum of the connections of a node, that is, the correlation coefficients. The strength centrality measure represents the probability that, when a symptom is found, the symptoms connected to that symptom will also be found.^{4,8}

Fig. 3 shows the strength of centrality of the items of the CES-D scale. The most central nodes are “I felt sad”, “I felt depressed”, “I felt that I could not shake off the blues even with help from my family and friends” and “I felt lonely”. Because the first three assess depressed mood, the most central symptoms of this network would be depressed mood and loneliness. Below these, there are symptoms related to anhedonia, such as “I could not get ‘going’” and “I enjoyed life”, so the results coincide with the core symptoms of depressive disorder in the DSM-V (sadness and anhedonia), but also includes loneliness as a central symptom, which does not appear in the diagnostic criteria of the DSM-V or the ICD-10,^{2,35} although other studies indicate that it could have an important role in the structure of depressive symptoms.^{28,36}

Fig. 4 shows the strength of centrality of the items of the ZDS scale in graph form. The most central nodes are “I feel downhearted and blue” and “I find living pleasant”, followed by “I feel useful and needed”. These items evaluate sadness, anhedonia and the feeling of worthlessness respectively. These three symptoms are included in the DSM-V criteria, and the first two are core symptoms.² Furthermore, the item “Morning is when I feel best about my sadness”, which represents a symptom of morning blues, is the least connected and furthest in the network, being also less central than the other symptoms. Morning blues was one of the specifier criteria for depression with melancholic features in the DSM-V,² and also a criterion for melancholia since the DSM-III.³² The low centrality of morning blues coincides with other studies in network analysis, such as those by Briganti et al.³⁷ and Fried et al.,³⁸ which indicates that its presence in psychometric instruments would not be so relevant.

The case-dropping bootstrap technique was used to determine the stability of the network. This technique assesses the stability of the most central items if the sample size was randomly reduced. Fig. 5 shows the stability of the central symptoms of the CES-D scale, which has regular stability by allowing a reduction in the sample size of 36.1% to maintain a correlation of 0.7 in the central symptoms with those of the original sample, with a 95%CI. Fig. 6 shows the stability of the central symptoms of the ZDS scale, which does not show adequate stability, as it only allows a 20.6% reduction in the sample size, while maintaining a correlation of 0.7 in the central symptoms with those of the original sample, with a 95%CI.²⁰

Limitations

The results of this study must be interpreted taking into account the limitations of a cross-sectional study that does not allow causal relationships to be demonstrated, so any connection represents only the strength of association between the symptoms. Furthermore, in network analysis, the choice of the model entails certain limitations that must be considered in relation to the objectives of the study, which in our case aimed to describe only the general structure of symptoms of the CES-D and ZDS.³⁹

Another problem often found in network analysis is that the scales used have more than one item that measures the same construct, so these items would have a strong

correlation, and their centrality measures would artificially increase.²⁶

Finally, sample size significantly affects the performance of network analysis. The network estimation model used in this study is the EBICglasso, a regularisation method that allows the elimination of spurious connections (connections with a tendency to zero), which facilitates the visualisation of a more parsimonious network.^{22,24} However, in the most recent literature on network analysis, non-regularised methods have had better performance,⁴⁰ although this was valid only for large sample sizes, so the EBICglasso method continues to be useful with small samples such as in this study.³⁹

Conclusions

The results indicate that sadness, loneliness, anhedonia and feelings of worthlessness are the most central symptoms of depressive disorder based on the CES-D and ZDS scales. Among these symptoms, there is a greater association between sadness and loneliness and between the feeling of worthlessness and anhedonia.

Somatic symptoms considered comorbid with anxiety, such as tachycardia, digestive discomfort and restlessness, are grouped in the periphery of the network, which suggests they could be considered bridge symptoms with anxiety disorder following the hypothesis of the depression-anxiety continuum.

Finally, morning blues does not represent a central symptom, so its relevance among the diagnostic criteria would be questionable.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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