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ORIGINAL ARTICLE

Do depressed people with subjective psychomotor retardation show a different symptomatic pattern? A network analysis approach using a cross-national sample

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KEYWORDS
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Abstract
Background and objectives: Psychomotor retardation (PMR) has been associated with worse clinical course in depressed people. Explanations for this finding remain inconclusive. This study aimed to analyse whether depressed people with subjective PMR might show a different symptomatic pattern and to describe their clinical and sociodemographic profiles.
Methods: A total of 1024 participants from Finland, Spain and Poland, part of the "COURAGE in Europe" Project who screened positive for a depressive episode according to International Classification of Diseases-10 (ICD-10) criteria using the World Health Organization Composite International Diagnostic Interview 3.0 (CIDI 3.0), were included. Two group networks of depressive symptoms were estimated according to the presence (555 people) and absence (469 people) of subjective PMR. Measures of strength and betweenness of depressive symptoms were explored.
Results: People with subjective PMR showed a higher number of symptoms (11.30 (±2.67) versus 9.26 (±2.77)) and global disability score (38.30 (±26.41) versus 19.59 (±19.31) than people without subjective PMR. Although no difference was found in the global structure (M-Test=1.531; p = 0.994) nor the global strength (S-Test=0.248; p = 0.954) of depressed symptoms between depressed people with and without subjective PMR, differences were found in the type of central symptoms; "Restlessness/Jitters" (p = 0.01) and "Early Wake-Up" (p = 0.02) were relevant for the subjective PMR group. These two symptoms worked as bridge items between other depressive symptoms specifically for depressed people with subjective PMR.
Conclusions: Our results confirm that subjective PMR in depression is associated with higher severity of symptoms and disability. Depressed People with subjective PMR might show a

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different pattern of nuclear symptoms. Suicidal attempt, early wake-up and restlessness could be high-priority targets in the treatment of depressed people with subjective PMR.

Introduction

Depression is currently one of the most important worldwide public health problems; approximately 280 million people in the world have depression, an estimated 3.8 % of the population, including 5 % of adults (4 % among men and 6 % among women), and 5.7 % of adults older than 60 years.[1]

One of the core symptoms of depression is psychomotor retardation (PMR).[2] PMR is defined by a set of symptoms and/or signs which are related to motor or cognitive impairments, or both. These include alterations of speech, facial expression and eye movements, as well as changes in self-touching, posture, and speed and degree of movements.[3] Assessment of psychomotor retardation has been typically conducted using interviewer-rated scales based on observable signs and symptoms. Depression rating scales often include a single item regarding the presence or absence of agitation and retardation which is open to subjective interpretation.[4] Other studies have objectively assessed psychomotor retardation using a range of measures including gait speed and timed fine motor tasks [5]; Both objective and subjective measures are relevant to clinical practice and, although they measure relatively different aspects, they are correlated.[6] Subjective PMR has been a factor associated with greater severity of depression. Therefore, self-reported scales also have been proven useful to determine the presence of psychomotor retardation in patients with depression and have been used to carry out studies on this topic.[7]

PMR in depression has been associated with worse treatment outcomes, recurrence and treatment resistance.[8] Some evidence shows that depressed people with PMR usually experience a higher severity of depression, but the reasons for this are still unclear. Literature reporting factors associated with PMR has not helped to clarify this question.[3] Some studies have found that this symptom tends to be present in less common types of depression which are relatively frequent in old people, such as depression-executive dysfunction syndrome.[9] However, other studies have shown that PMR in depressed geriatric patients is similar in anatomical and functional characteristics to PMR in younger adults.[10] Similarly, some studies have found no clinically relevant gender differences in the prevalence of any psychomotor symptoms,[11] whereas other studies have informed higher rates of retardation in males than females.[12]

Network analysis has been developed as an innovative alternative approach to conceptualizing psychiatric pathologies. In the network model, the disorders are assembled as networks arising from interactions between symptoms; these interactions explain the development and maintenance of mental disorders rather than passively reflecting the latent cause.[13] The network is made up of two key elements: the nodes (which represent the symptoms) and the edges (associations between symptoms).[14]

According to network theory, central symptoms feature the most connections with others and can trigger or change other manifestations. Thus, defining the central symptoms could have relevant clinical implications for developing adequate focused interventions to treat psychiatric disorders.[13] Fatigue and sad mood have been consistently identified as central symptoms of Major Depressive Disorder (MDD) using network analyses.[15]

However, no study to our knowledge has analysed whether depressed people with subjective PMR might have a different structure of depressive symptoms than depressed people with no subjective PMR. Therefore, this study aims to shed light on improving treatments for depressed people with subjective PMR investigating whether these might show different nuclear depressive symptoms and analysing whether they have a distinct sociodemographic and clinical profile than depressed people without subjective PMR. We hypothesised that 1) depressed people with subjective PMR would have higher severity and higher disability as previous literature has reported and 2) the key depressive symptoms for the subjective PMR depressed group would be different; symptoms related to slowness (such as slow thinking, lack of energy) and higher clinical severity (such as suicide thoughts and suicide attempts) would show a higher centrality.

Methods

Participants

This work is a secondary analysis of the "Collaborative Research on Ageing in Europe" ("COURAGE in Europe") study. Data collection was conducted in 2011. Face-to-face interviews were performed by trained interviewers at the homes of individuals randomly sampled from the non-institutionalized adult population (18+) of Finland (n = 1976), Poland (n = 4071) and Spain (n = 4753) based on the multistage clustered design. All the study's interviewers received standardized training. Quality assurance procedures were also implemented during fieldwork.[16] The response rate was 53.4 % for Finland, 66.5 % for Poland and 69.9 % for Spain. Countries were selected to give a broad representation across different European regions with different populations and different health characteristics.[17] The present study was approved by the Ethical Committee of Neurological Institute Carlo Besta, Milan, Italy, project coordinator; the Ethics Review Committee, National Public Health Institute, Helsinki, Finland; the Bioethical Committee, Jagiellonian University, Krakow, Poland; Ethics Review Committee, Parc Sanitari Sant Joan de Déu, Barcelona, Spain; and Ethics Review Committee, La Princesa University Hospital, Madrid, Spain. The authors were responsible for ensuring that the study was conducted by the standards contained in the Declaration of Helsinki. Informed consent was obtained from

people before their inclusion in the primary project, after receiving the whole information.

This study was composed of a subsample of 1024 adult people with a self-reported 12-month depressive episode diagnosed by a health professional and/or who screened positive for depressive episode according to the International Classification of Diseases-10 (ICD-10) criteria[18] by using an adapted version of the Composite International Diagnostic Interview (CIDI 3.0).[19] The CIDI 3.0 instrument has shown good diagnosis agreement among clinicians and trained interviewers.[19]

Measurements

Psychomotor retardation

Subjective Psychomotor Retardation was measured as a binary variable (Yes/No) using the question "¿Did you notice slowness when you moved from one place to another?" which is part of the adapted version of the CIDI 3.0 interview.[19] A positive answer to this question was used to determine its presence.

Presence of 12-month depressive symptoms

Information on the presence of 15 different depressive symptoms (Yes/No) in the last 12 months before the interview was included from the adapted version of the CIDI 3.0 interview.[19] These questions included: sad mood, loss of interest, lack of energy, loss of appetite, slow thinking, difficulty falling asleep, early wake-up, difficulty concentrating, anxiety/worry, restlessness/jitters, low self-esteem, hopelessness, loss of interest in sex, suicidal thoughts, and suicide attempts.

Sociodemographic variables

The sociodemographic variables of interest were age (participants were classified into two groups: "18—49 years old" and "+50 years old"), gender (male/female), marital status (married or in partnership/not married nor in partnership) educational level (less than Primary, completed Primary, completed Secondary, completed High School, completed University or higher), and low household income including country-specific quintiles of household income (low household income: 1st and 2nd quintiles/no low household income: 3rd, 4th and 5th quintiles).

Severity of depressive episode

The number of depressive symptoms reported by the participant in the CIDI 3.0 depression module [18] was used as an indicator of the severity of depression. A higher number of symptoms meant a higher severity of depressive episode.

Disability

The 12-item World Health Organization Disability Assessment Schedule II (WHO-DAS II) was used to measure the degree of disability of depressed people. WHO-DAS II is a practical, generic assessment instrument that can measure disability at the population level or in clinical practice. WHO-DAS II captures the level of functioning in six domains of life: cognition, mobility, self-care, getting along, life activities and participation. A complex scoring indicated in the WHODAS manual was used to calculate a final global disability score which ranges from 0 to 100, representing the highest disability.[20]

Statistical analysis

Firstly, descriptive analysis was conducted to detail the sociodemographic and clinical features of both groups related to variables of interest. To do so, means and standard deviations were calculated for quantitative variables; frequencies and proportions were calculated in the case of categorical variables. Secondly, group comparisons were conducted to estimate possible demographic, symptomatic and disability differences between depressed people with and without subjective PMR. Student *t*-tests for independent samples were used in the case of quantitative variables, whereas Chi-Square tests were employed for categorical variables.

To explore the importance of each depressive symptom as well as the relationships between them in both groups, network analyses were conducted. One network was performed for each group. As the used data were binary, the networks were performed using the Ising model, a binary equivalence of the Gaussian approximation method.[21] The regularization method "Least Absolute Shrinkage and Selection Operator" (LASSO) was applied to limit the number of spurious connections. This tool restricts the total sum of absolute parameter values, leading many edge estimates to shrink to exactly zero and abandoning the model.[22] To obtain the best result, the value of this regularization (Extended Bayesian Information Criterion (EBIC)) was fixed at γ= 0.25.

To measure the relative importance of each node (symptom) within the network structure, two centrality indices were calculated: node strength (the sum of absolute edge weights connected to each node) and betweenness (how often one node is in the shortest paths between other nodes). The higher the values in these assessments, the more important the nodes are in the network.[22] The symptom "sad mood" was not included in the network analysis due to the lack of variability between both groups.

Additional analyses were performed to check the robustness of the network; confidence intervals on the edge weights under the bootstrapping technique and the *Correlation Stability Coefficient* were estimated.[23] The latter represents the maximum proportion of cases that can be dropped to retain a correlation of at least 0.7 with the original centrality indices.

Finally, to compare network structures between the two participant groups, the *Network Comparison Test* was used. This test examined three hypotheses: invariant network structure (both groups have the same network structure), invariant edge strength (the strength of a particular edge is the same in both groups) and invariant global strength (the overall level of connectivity is equal across groups).[24]

A *p-value* of less or equal to 0.05 ($p \leq 0.05$) was used as the significance threshold in this study. Descriptive and univariant analyses were performed in the statistical package SPSS 27.0 for Windows.[25] Network analysis was performed using the "IsingFit"[26] and "NetworkComparisonTest" [27] RStudio packages.

Results

Sample description

The number of participants was 1024. The mean age was 60.97 (±15.34) and 82.2 % were older than 50 years. 71.7 %

Table 1 Sociodemographic features of the sample.

Sociodemographic variables		Total Sample N = 1024	No PMR Group N = 469	PMR Group N = 555	Statistical Values
Age		60.97 (±15.34)	58.34 (±15.80)	63.18 (±14.58)	t = 5.06 p<0.001
Age (By Group)	18—49 years old	182 (17.8 %)	106 (22.6 %)	76 (13.7 %)	χ^2=13.20
	50+ years old	842 (82.2 %)	363 (77.4 %)	479 (86.3 %)	p<0.001
Gender	Women	734 (71.7 %)	328 (69.9 %)	406 (73.2 %)	χ^2=1.14
	Men	290 (28.3 %)	141 (30.1 %)	149 (26.8 %)	p = 0.28
Marital Status	Married or in partnership	476 (46.5 %)	231 (49.3 %)	245 (44.1 %)	χ^2=2.50
	Not married nor in partnership	548 (53.5 %)	238 (50.7 %)	310 (55.9 %)	p = 0.12
Educational Level	Less than Primary	288 (28.1 %)	114 (24.3 %)	174 (31.4 %)	χ^2=33.78
	Completed Primary	255 (24.9 %)	91 (19.4 %)	164 (29.5 %)	p<0.001
	Completed Secondary	144 (14.1 %)	71 (15.1 %)	73 (13.2 %)	
	Completed High School	220 (21.5 %)	128 (27.3 %)	92 (16.6 %)	
	Completed University or higher	117 (11.4 %)	65 (13.9 %)	52 (9.4 %)	
Country	Finland	135 (13.2 %)	72 (15.4 %)	63 (11.4 %)	χ^2=3.70
	Poland	288 (28.1 %)	126 (26.9 %)	162 (29.2 %)	p = 0.16
	Spain	601 (58.7 %)	271 (57.8 %)	330 (59.5 %)	
Low Household Income (1st and 2nd quintile)	No	461 (47.6 %)	226 (51.2 %)	235 (44.6 %)	χ^2=4.00
	Yes	507 (52.4 %)	215 (48.8 %)	292 (55.4 %)	p = 0.045

of the participants were women, and 53.5 % were married or in partnership. All the basic characteristics of the total sample can be found in Table 1.

Demographic and clinical differences by psychomotor retardation groups

Demographic, clinical, and disability comparisons among depressed people with subjective PMR and without subjective PMR are reported in Tables 1 and 2. Subjective PMR was associated with older age (t(962.9)=5.06; p<0.001) (χ^2(1) =13.20; p<0.001), lower educational level (χ^2(4)=33.78; p<0.001) and lower income (χ^2(1)=4.00; p = 0.045).

In addition, depressed people who suffered from subjective PMR showed higher global disability (t(993.9)=13.01; p<0.001) and a higher number of depressive symptoms (t(965.3)= 11.93; p<0.001) (see Table 2). Regarding the presence of depressive symptoms individually, the subjective PMR group showed a higher prevalence of all screened depressive symptoms with the exception of sad mood (χ^2(1) =1.69; p = 0.19) and suicide attempt (χ^2(1)=2.85; p = 0.09).

Are there any differences in the general structure and relationships of depressive symptoms between people with and without PMR?

The estimated networks for both groups can be seen in Fig. 1. Some depressive symptoms in the subjective PMR group network showed negative correlations (between suicidal attempt and anxiety, loss of sexual interest, and hopelessness), whereas the rest were positive. In the case of the No subjective PMR group network, there were negative correlations between suicidal attempt and jitters, anxiety, early wake-up, slow thinking, and lack of interest; also between suicidal thoughts and lack of interest, early wake-up, and loss of appetite, and finally between anxiety and difficulty to fall asleep. When comparing both subjective PMR and No subjective PMR networks, there were no significant differences in global strength (S-Test=0.248; p = 0.954) or global structure (M-Test=1.531; p = 0.994). However, there were significative variations between subjective PMR and No subjective PMR groups in certain edge strengths: the connections between low self-esteem and hopelessness (p = 0.002) and between jitters and suicide attempt (p = 0.007).

Are there any differences in the relevant depressive symptoms between people with and without PMR?

The centrality indices (strength and betweenness) of each symptom in both groups are represented in Fig. 2. According to the observable values, the node with the highest strength centrality in the subjective PMR network was “suicidal attempt”, followed by “suicidal thoughts” and “lack of interest”, whereas in the No subjective PMR network were “suicidal attempt” and “suicidal thoughts”. Regarding the betweenness centrality, the most important nodes in the subjective PMR network were “suicidal attempt”, “jitters/restlessness” and “early wake-up”, while in the No subjective PMR network were “suicidal attempt” and “suicidal thoughts”. Taking into account both values, the key symptoms for the subjective PMR group were “suicide attempt”, “early wake-up” and “jitters”. Instead, the most important symptoms for the No subjective PMR group were “suicide attempt” and “suicidal thoughts”. These tendencies are especially determined by the betweenness, given that strength values are quite similar in both groups. Regarding measures of centrality, there are no significant differences related to strength. Nonetheless, there are two significative discrepancies in the betweenness of specific nodes: early wake-up (p = 0.02) and jitters (p = 0.01).

Table 2 Clinical features of the sample.

Clinical Variables		No PMR Group	PMR Group	Statistical Values
Global Disability Score (WHO-DAS II 12-Item Version)		19.59 (±19.31)	38.30 (±26.41)	t = 13.01 p<0.001
Sad Mood	YES	438 (93.4 %)	505 (91.0 %)	χ^2=1.69
	NO	31 (6.6 %)	50 (9.0 %)	p = 0.19
Loss of interest	YES	396 (84.4 %)	495 (89.2 %)	χ^2=4.67
	NO	73 (15.6 %)	60 (10.8 %)	p = 0.03
Lack of energy	YES	413 (88.1 %)	541 (97.5 %)	χ^2=33.94
	NO	56 (11.9 %)	14 (2.5 %)	p<0.001
Loss of appetite	YES	221 (47.1 %)	363 (65.4 %)	χ^2=33.94
	NO	248 (52.9 %)	192 (34.6 %)	p<0.001
Slow thinking	YES	240 (51.3 %)	452 (81.4 %)	χ^2= 104.14
	NO	228 (48.7 %)	103 (18.6 %)	p<0.001
Difficulty falling asleep	YES	324 (69.1 %)	447 (80.5 %)	χ^2=17.33
	NO	145 (30.9 %)	108 (19.5 %)	p<0.001
Early wake-up	YES	270 (57.6 %)	417 (75.1 %)	χ^2=34.73
	NO	199 (42.4 %)	138 (24.9 %)	p<0.001
Difficulty to concentrate	YES	287 (61.2 %)	491 (88.5 %)	χ^2=102.11
	NO	182 (38.8 %)	64 (11.5 %)	p<0.001
Anxiety/Worry	YES	389 (82.9 %)	507 (91.4 %)	χ^2=15.67
	NO	80 (17.1 %)	48 (8.6 %)	p<0.001
Restlessness/Jitters	YES	278 (59.3 %)	414 (74.6 %)	χ^2=26.53
	NO	191 (40.7 %)	141 (25.4 %)	p<0.001
Low Self-Esteem	YES	314 (67.0 %)	473 (85.2 %)	χ^2=46.70
	NO	155 (33.0 %)	82 (14.8 %)	p<0.001
Hopelessness	YES	307 (65.5 %)	469 (84.5 %)	χ^2=49.20
	NO	162 (34.5 %)	86 (15.5 %)	p<0.001
Loss of interest in sex	YES	259 (56.1 %)	392 (70.8 %)	χ^2=23.00
	NO	203 (43.9 %)	162 (29.2 %)	p<0.001
Suicidal Thoughts	YES	160 (34.1 %)	244 (44.0 %)	χ^2=9.91
	NO	309 (65.9 %)	311 (56.0 %)	p = 0.002
Suicidal Attempt	YES	31 (6.6 %)	54 (9.7 %)	χ^2=2.85
	NO	438 (93.4 %)	501 (90.3 %)	p = 0.09
Total of Symptoms		9.26 (±2.77)	11.30 (±2.67)	t = 11.93 p<0.001

Stability of results

The stability of betweenness was low for both subjective PMR (r for betweenness =0.00; r for strength = 0.206) and No subjective PMR groups (r for betweenness = 0.00; r for strength = 0.200); however, the strength values were slightly better for both groups. These sensitivity results are presented in Figs. 3 and 4.

Discussion

This study aimed to show whether depressed people with subjective PMR presented a different clinical and sociodemographic profile compared to those with no subjective PMR. Furthermore, it is focused on showing how depressive symptoms are interrelated and what their relevance is according to the presence of subjective PMR in this pathology.

In line with our initial hypothesis, our results showed that people with subjective PMR experienced a higher number of symptoms and higher disability. These findings are consistent with previous literature; Rakofsky et al. (2013) described that depressed people with PMR usually experience a higher severity of depression [28] and Peng et al. (2022) related the presence of PMR with a higher disability in depressed people.[29]

Congruently also to previous studies, our results showed that PMR was associated with older age; this finding has been explained among others alluding ageing related factors.[9] In addition, lower education, and lower household income, were related to the presence of subjective PMR. The cross-sectional nature of this study does not allow giving clear explanations for these findings; however, people with lower education levels and lower incomes may have a risk of more severe symptomatic depression. It could also be that they simply tend to respond more frequently with "yes" to all depressive symptoms, due to a "halo effect" and/or to the greater difficulty of comprehensively understanding nuances of all questions in a survey. This would also explain the worse prognosis of this group found in the previous literature.[8]

Our study additionally analysed whether depressed people with subjective PMR might present differences in the

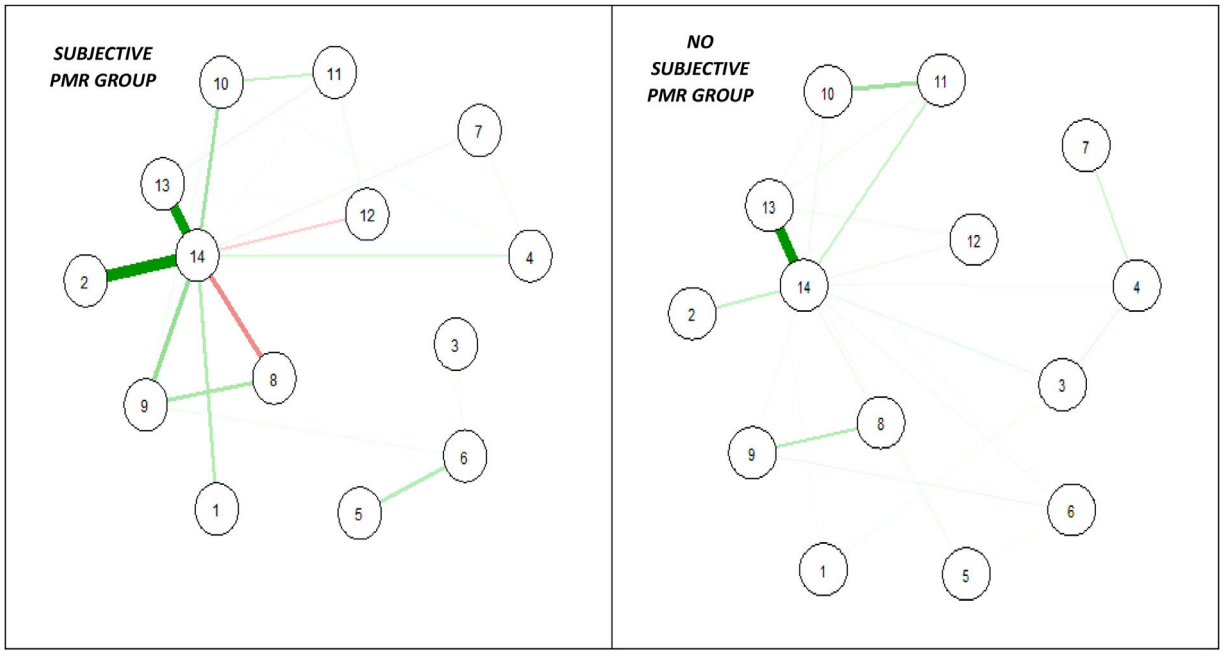

Fig. 1 Network analysis graph of both groups. 1= loss of interest; 2= lack of energy; 3=loss of appetite; 4= slow thinking; 5=difficulty to fall asleep; 6=early wake up; 7= difficulty to concentrate; 8=anxiety/worry; 9=restlessness/ jitters; 10=low self-esteem; 11=hopelessness; 12=loss of sexual interest; 13= suicidal thoughts; 14=suicidal attempt. "Sad mood" symptom was not included due to the lack of variability between both groups. The thickness and colour intensity of the edges represent the magnitude of the association. Green edges represent positive relationships, while red edges represent negative relationships.

structure and relationships of depressive symptoms. It showed neither differences in the global strength nor the structure of networks among depressed people with and without subjective PMR. Given these negative main results, perhaps there could be other potentially explanatory underlying mechanisms different from PMR that might be more determinant in categorizing depressive endophenotypes with more certainly differentiated manifestation structures and considerably distinct prognoses. For example, the side effects of antidepressants could be an interesting

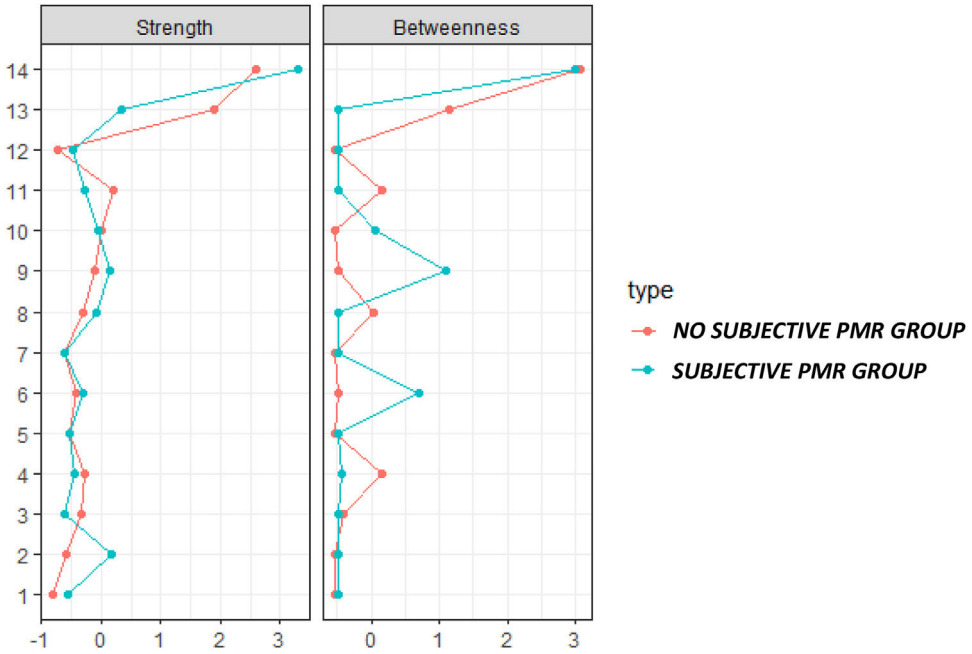

Fig. 2 Measures of centrality of both groups from network analysis. 1= loss of interest; 2= lack of energy; 3=loss of appetite; 4= slow thinking; 5=difficulty to fall asleep; 6=early wake up; 7= difficulty to concentrate; 8=anxiety/worry; 9=restlessness/ jitters; 10=low self-esteem; 11=hopelessness; 12=loss of sexual interest; 13= suicidal thoughts; 14=suicidal attempt. "Sad mood" symptom was not included due to the lack of variability between both groups.

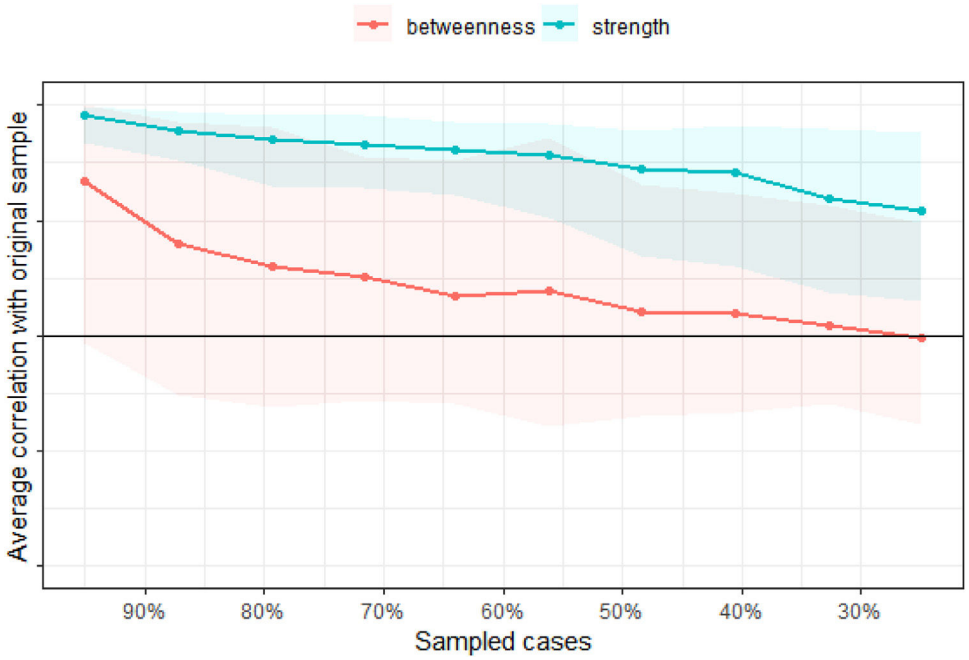

Fig. 3 Stability of the centrality measures of the No subjective PMR Group estimated by case dropping subset bootstrapped method. This figure represents the maximum proportion of cases that can be discarded to maintain a correlation of at least 0.7 with the centrality measures of the original network. The lines represent the mean of the correlation while the areas represent the range.

variable to study with this objective. Nonetheless, the networks cannot be controlled by variables that are not part of the network itself. Further studies should explore more underlying mechanisms that might be potentially relevant to differentiate depressive endophenotypes in the future.

Our results revealed that people with subjective PMR might have different nuclear depressive symptoms as well as different relationships between them when compared to those without this symptom. In contrast to the No subjective PMR group, "early wake-up" and "jitters/restlessness" were key symptoms for the subjective PMR group. Literature shows that about three-quarters of depressed patients might suffer from early wake-up.[30] McCall et al. (2023) have already found that higher insomnia was related to slower

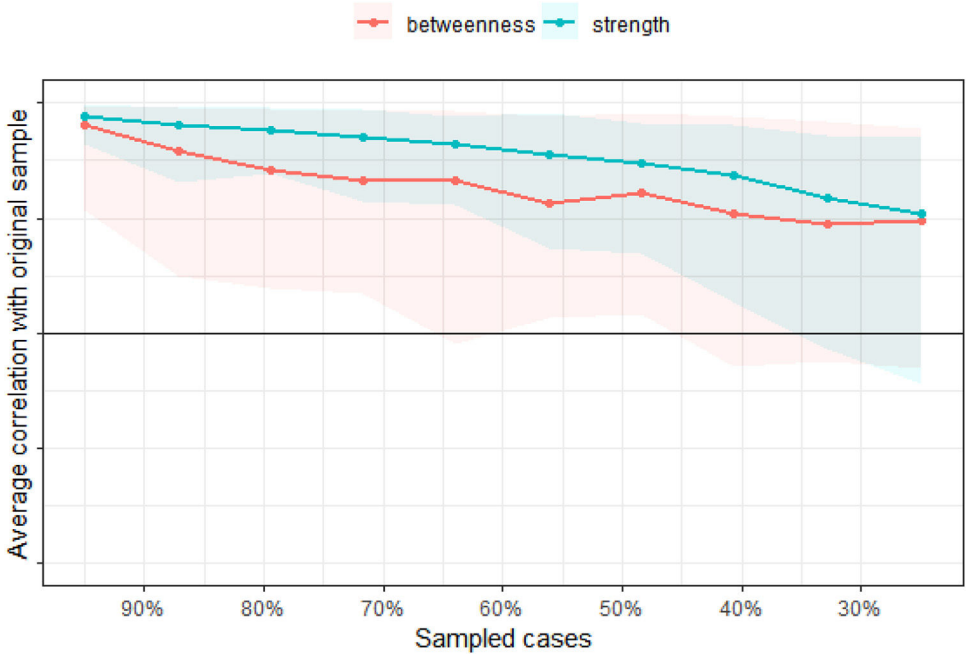

Fig. 4 Stability of the centrality measures of the subjective PMR group estimated by case dropping subset bootstrapped method. This figure represents the maximum proportion of cases that can be discarded to maintain a correlation of at least 0.7 with the centrality measures of the original network. The lines represent the mean of the correlation while the areas represent the range.

psychomotor speed.[31] In fact, insomnia and psychomotor retardation have been both categorized under the "somatic" category [32] of depressive symptoms. Furthermore, this finding could be explained by the presence of the melancholic subtype of depression. Melancholic depression has been viewed as the most serious subtype of major depressive disorder and features specific clinical symptoms, such as persistent anhedonia, psychomotor disturbances, cognitive impairment, early morning awakening, excessive guilt, and anorexia.[33] However, recently, the melancholia concept has been put into doubt by some clinicians and researchers who consider there is not enough homogeneity in the patients' manifestations diagnosed under this subtype. Our study has additionally found that it is early wake-up and not problems related to starting sleep which seems to be more relevant in the subjective PMR group. This result should be further explored.

Regarding the importance of "jitters/restlessness" symptoms for depressed people with subjective PMR, it would be a surprising result if we considered that psychomotor retardation and agitation are apparently mutually exclusive. However, some authors consider that PMR is only one expression among others within a broader activity disorder.[34] The inclusion of motor retardation and agitation into the same dimensional category might explain the fact that decreased facial expressions have been often coupled with gross motor restlessness and increased hand movements, specifically in patients with severe depression.[35] Thus, specific instruments employed for identifying and assessing psychomotor retardation should be designed to capture the presence of both phenomena.

Interestingly, "Suicide thoughts" showed a higher importance in the No subjective PMR group, whereas it was not a central symptom in the subjective PMR group. Contrary to our results, previous network analyses have shown that suicidal ideation had the strongest correlation with psychomotor retardation/agitation in domestic workers [35] and depressed nursing students.[36] The fact that our study has been conducted in the general population and using different instruments might explain these differences.

On the other hand, our study found a significant difference in the strength edge of the relationship that connects "suicide attempt" and "restlessness-jitters", this link being stronger in the subjective PMR group. The alterations found in the prefrontal cortex of depressed people with PMR [37] together with their strong connection with suicide attempts and not with suicide ideation may suggest that depressed people with PMR might present different suicide behaviours in terms of impulsiveness and planning. To our knowledge, no studies have previously tested if depressed populations with subjective PMR experience more impulsivity in their suicide attempts which could be very useful in terms of suicide prevention plans.

Finally, our results did not confirm our initial hypothesis that all somatic symptoms of depression (lack of energy and most importantly cognitive slowness) were strongly interconnected in depressed people within the subjective PMR group.

The results of the present study might have clinical implications as they show that, in depressed people with subjective PMR, interventions focused on suicide attempts, restlessness and early wake-up could be high-priority, since they appear to be impactful in the rest of depressive symptoms. Currently, electroconvulsive therapy is one of the most effective therapeutic tools for depressed people with PMR.[38] Therefore, it is a highly recommended treatment for the targeted population in this study. Besides this, identifying central depressive symptoms for the PMR group might help to postulate additional treatment options with easier access. Physical exercise is a good option for these people since it has been associated with decreased restlessness symptoms [39] and higher quality of sleep.[40] Combined exercise and antidepressant therapy have shown higher efficiency for depressed people with PMR than antidepressant therapy alone.[41] Further studies are needed to explore if these results can be replicated in depressed people with subjective PMR specifically. Finally, used alongside pharmacotherapy and/or psychotherapy, massage therapy might be a promising therapeutic tool for this patient profile; it could help relieve depressive somatic symptoms such as psychomotor retardation and restlessness, and improve sleep quality, especially difficulty remaining asleep.[42] However, the literature available about its use and effectiveness in depressed people is still scarce; therefore, further studies are required to explore this therapeutic option.

This work has also some limitations. First, due to the cross-sectional study design, causal relationships between these depressive symptoms and dynamic changes in symptom networks over time could not be established. Further studies with longitudinal design are needed to confirm the links that have been described in this investigation. Secondly, data from some variables, including PMR, were collected by self-reported questions which are open to subjective interpretation. Beyond this, it was based on a dichotomous determination and not dimensional. Further studies should use more specific tools of psychomotor retardation and confirm the results shown in our work. The use of self-reported information could increase the risk of desirability bias and recall bias, which are probably the most important linked to this type of data. However, previous research has also shown that subjective measures of depressive symptoms are useful and should not be underestimated in the treatment outcomes.[43] Furthermore, if interviews were conducted by health professionals, they could have provided more accurate information. Nonetheless, our study carried out a standardized process and quality control to ensure we were collecting reliable information, as described in the Methods section. Finally, we acknowledge that the measure of severity of depression is more complex than the number of reported symptoms.

In spite of these limitations, this is the first study that has used the network analysis approach to examine the relationships between depressive symptoms according to the presence of subjective PMR in people with depression. The results indicated that "Suicide Attempt", "Early wake-up" and "Jitters" are the most important symptoms for people with subjective PMR. As such, these manifestations should be prioritized as the targets in treatment and prevention interventions for depression among the European adult population with this symptom. Further studies to confirm these findings and their application to clinical practice are required.

Author contributions

J.G.C drafted the first version of the manuscript with the help of A.I. and M.C; A.I. performed the statistical analyses and interpreted the results; B.T.A, S.K., J.M.H. and JL.A.M. designed the study and coordinated all aspects of the study implementation and data collection; and A.I., B.T.A,S.K., J. M.H., J.L.A.M. and M.C. reviewed the manuscript for important intellectual content and approved the final version as submitted. All authors have read and agreed to the published version of the manuscript.

Ethical considerations

The present study was approved by the Ethical Committee of Neurological Institute Carlo Besta, Milan, Italy, project coordinator; the Ethics Review Committee, National Public Health Institute, Helsinki, Finland; the Bioethical Committee, Jagiellonian University, Krakow, Poland; Ethics Review Committee, Parc Sanitari Sant Joan de Déu, Barcelona, Spain; and Ethics Review Committee, La Princesa University Hospital, Madrid, Spain. The authors were responsible for ensuring that the study was conducted by the standards contained in the Declaration of Helsinki. Informed consent was obtained from people before their inclusion in the primary project, after receiving the whole information.

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Conflicts of interest

None.

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