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A body-mind map

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The network structure of major depressive disorder, generalized anxiety disorder and somatic symptomatology

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ABSTRACT

Introduction: Major depressive disorder (MDD) and generalized anxiety disorder (GAD) often co-occur with somatic symptomatology. Little is known about the contributions of individual symptoms to this association. More insight into their relations could help to identify symptoms that are central in the processes behind the co-occurrence. This study explores associations between individual MDD/GAD symptoms and somatic symptoms by using the network approach.

Methods: MDD/GAD symptoms were assessed in 2,704 participants (mean age 41.7 years, 66.1% female) from the Netherlands Study of Depression and Anxiety (NESDA) using the Inventory of Depressive Symptomatology (IDS). Somatic symptoms were assessed with the somatization scale of the Four-Dimensional Symptom Questionnaire (4DSQ). The technique eLasso was used to estimate the network of MDD/GAD and somatic symptoms.

Results: The network structure showed numerous associations between MDD/GAD and somatic symptoms. In general, neurovegetative and cognitive/affective MDD/GAD symptoms showed a similar strength of connections to the somatic domain. However, associations varied substantially across individual symptoms. MDD/GAD symptoms with many and strong associations to the somatic domain included anxiety and fatigue, whereas hypersomnia and insomnia showed no connections to somatic symptoms. Among somatic symptoms, excessive perspiration and pressure/tight feeling in chest were associated with the MDD/GAD domain, while muscle pain and tingling in fingers showed only a few weak associations.

Conclusions: Individual symptoms show differential associations in the co-occurrence of MDD/GAD with somatic symptomatology. Strongly interconnected symptoms are important in furthering our understanding of the interaction between the symptom domains, and may be valuable targets for future research and treatment.

INTRODUCTION

Major depressive disorder (MDD) and generalized anxiety disorder (GAD) are prevalent and debilitating [150,166]. The conditions are strongly connected as their symptoms frequently co-occur and show strong overlap [40,74]. Consequently, comorbidity rates between the disorders have been reported to be as high as 40-60% [229].

Previous studies have shown that MDD and GAD are associated with higher levels of somatic symptomatology [44,45,79,197]. A study of our own group, for example, demonstrated that patients with MDD or GAD have a 1.5-3 times higher risk of suffering from certain clusters of somatic symptoms than persons without those disorders [197]. However, as these studies have mainly used instruments based on diagnoses or scale scores, it is unclear whether individual MDD/GAD and somatic symptoms contribute equally to this association. It could be that only specific symptoms of MDD/GAD are related to somatic symptoms and vice versa. Such symptoms are called bridging symptoms [84] and they may be a valuable focus for future research in order to disentangle the general co-occurrence of MDD/GAD with somatic symptomatology. In addition, targeting treatment to bridging symptoms may help to improve the outcomes of MDD/GAD patients with somatic symptoms.

MDD/GAD symptoms are often classified into symptoms that are physical in nature (i.e., *neurovegetative symptoms* such as fatigue and insomnia) and symptoms that refer to cognition or mood (i.e., *cognitive/affective symptoms* such as depressed mood or anxiety). Neurovegetative symptoms are well-known to be associated with somatic symptomatology as these types of symptoms can be the result of the same somatic diseases or physical dysregulations (e.g., heart failure can cause fatigue as well as shortness of breath). In addition, neurovegetative symptoms show strong reciprocal relations with somatic symptoms (e.g., insomnia can cause the somatic symptom headache and vice versa) [230]. Cognitive/affective symptoms, however, are more strongly related to mental processes [93] and, consequently, could show only weak connections to somatic symptomatology [231]. Despite these general patterns, individual symptoms of MDD/GAD as well as individual somatic symptoms may also be differentially related with one another. Of neurovegetative MDD/GAD symptoms, for example, psychomotor agitation may be associated with somatic symptoms such as palpitations and excessive perspiration, whereas hypersomnia may not be connected to any somatic symptom.

The network approach is a conceptualization of psychopathology and related conditions that concentrates on individual symptoms and their associations [84]. In this approach, symptoms are represented as nodes and the associations between them as edges. Symptoms of multiple diagnoses or domains can be combined into one network

structure, which, consequently, offers the opportunity to study the patterns in which these symptoms co-occur [74]. In a recent study, for example, Boschloo et al. [232] presented the network structure of emotional and behavioral symptoms in preadolescents and revealed that depressive, anxiety, and somatic symptoms were related via a complex constellation of connections. While specific depressive and anxiety symptoms were strongly associated with somatic symptoms, others showed no connections at all, and individual somatic symptoms showed similarly differential associations. Although Boschloo et al. [232] did not include DSM symptoms of MDD/GAD and the number of somatic symptoms was limited, their findings indicate that combining MDD/GAD and somatic symptoms in a network structure could help to identify the bridging symptoms in their co-occurrence.

This study aims to examine the relations between individual MDD/GAD symptoms and somatic symptoms in a large sample (N=2,704) using the network approach. First, we explore the general structure of the network. Then, we specifically focus on associations between individual MDD/GAD symptoms and somatic symptoms. It is hypothesized that neurovegetative symptoms are more strongly interconnected with somatic symptoms than cognitive/affective symptoms. However, associations between the MDD/GAD and somatic symptom domain may differ across individual symptoms.

METHODS

Sample

Data were derived from the baseline assessment of the Netherlands Study of Depression and Anxiety (NESDA), an ongoing cohort study aimed at examining the long-term course and consequences of depressive and anxiety disorders in adults (18-65 years). A total of 2,981 participants were included for the baseline assessment in 2004-2007, consisting of 652 (22%) healthy controls with no lifetime depressive and/or anxiety disorder, 1,411 (47%) participants with a past-month diagnosis of a depressive and/or anxiety disorder and 918 (31%) participants with a prior history of a depressive and/or anxiety disorder (diagnoses were established with the Composite International Diagnostic Interview [CIDI] version 2.1 [173]). Recruitment took place in the community (19%), primary care (54%) and specialized mental health care (27%). Community-based participants had previously been identified in a population-based study, and primary care participants were identified through a three-stage screening procedure (involving the Kessler 10 scale [206] and the short-form CIDI by phone) conducted among a random sample of consulting patients of 65 general practitioners. Mental health care participants were recruited consecutively when newly enrolled at 1 of the 17 participating mental health

organization locations. Persons with insufficient command of the Dutch language or a primary clinical diagnosis of psychotic disorder, obsessive-compulsive disorder, bipolar disorder or severe substance use disorder were excluded. The research protocol was approved by the Ethical Committee of the three participating universities and all participants gave written informed consent. A detailed description of the NESDA study design can be found elsewhere [172].

For the present study, participants with any missing data on MDD/GAD or somatic symptoms (N=277, 9.3%) were excluded, resulting in a total sample of 2,704 persons. Participants with complete data were younger (41.7 [SD=13.1] versus 43.5 [SD=12.6] years, $p=.03$), received education for a longer period (12.2 [SD=3.2] versus 11.5 [SD=3.5] years of education, $p=.001$), and were less likely to have past-month MDD (25.8% versus 37.9%, $p<.001$) or GAD (12.7% versus 19.1%, $p=.004$), but did not differ with respect to gender (66.1% versus 69.3% female, $p=.29$) from participants with missing data.

DSM-IV symptoms of MDD/GAD

The frequency/severity of fourteen DSM-IV MDD and/or GAD symptoms [40] during the past week was assessed with the Inventory of Depressive Symptomatology self-report version (IDS-SR₃₀ [233,234]). As in prior studies [235-237], the criteria weight/appetite change, sleep change, and psychomotor change were disaggregated in an increase (i.e., weight/appetite increase, hypersomnia, and psychomotor agitation) or decrease (i.e., weight/appetite decrease, insomnia, psychomotor retardation). In addition, the symptoms loss of interest/pleasure, weight/appetite increase, weight/appetite decrease, and insomnia were composed from multiple items [236,237]. Based on dimensions identified in previous studies [76,77], all symptoms were classified as either neurovegetative (i.e., physical in nature) or cognitive/affective (i.e., mental in nature). An overview of all neurovegetative and cognitive/affective symptoms and their corresponding IDS items is included in **Supplementary Table 1**.

Symptoms were scored from 0 (absent) to 3 (frequent and/or severe) based on clearly stated anchors. However, the assumption of normality, which network estimation techniques for polytomous items (e.g., those based on partial correlations) rely on, was not satisfied in our data. Therefore, we dichotomized item-scores into either absent (score 0) or present (scores 1-3) and used a network estimation technique for binary data. The symptoms composed from multiple items were considered present when at least one of these symptoms was scored with ≥ 1 .

Somatic symptoms

The frequency of 16 somatic symptoms (e.g., cardiopulmonary, musculoskeletal, and gastrointestinal symptoms) during the past week was scored from 1 (never) to 5 (often)

with the somatization scale of the Four-Dimensional Symptom Questionnaire (4DSQ [174]). Similar to the MDD/GAD items, the somatic items were recoded as absent (score of 1) or present (scores 2-5) as they were not normally distributed.

Statistical analysis

Main analyses

To estimate the network structure of the binary MDD/GAD and somatic symptoms, eLasso (available as the package 'l1net' in R [238]) was used. eLasso uses l_1 -regularized logistic regression to identify associations between symptoms, adjusted for all other symptoms in the network. In this procedure, logistic regression analyses are performed to determine associations between items and, then, an l_1 -penalty is imposed on the regression coefficients to identify models with an optimal balance between parsimony and goodness of fit [239]. To find the best fitting model, the extended Bayesian information criterion is used to assess goodness of fit [240]. As a result, eLasso identifies an accurate estimate of the network structure while it avoids multiple testing problems that would arise with significance testing in networks with many nodes [238]. Based on the estimated symptom associations, a weighted, undirected graph was visualized using package 'qgraph' [241] in R. In a network structure, nodes (circles) represent symptoms and edges (lines) represent associations between symptoms. Green edges indicate positive associations and red edges represent negative associations. The thickness of edges indicates the connection weight estimated by eLasso. The layout of the graph was based on the Fruchterman-Reingold algorithm, which iteratively computed the optimal layout; symptoms with stronger and/or more connections were placed closer to each other [242].

First, we explored the general structure of the network. To examine the general connectivity of the network, the density of the network was calculated by determining the proportion of actual connections over the number of potential connections between all symptoms [243]. Subsequently, we focused on associations connecting the MDD/GAD symptom domain with the somatic symptom domain. To examine the strength of all connections from an individual symptom to all symptoms of the opposite symptom domain (i.e., for an MDD/GAD symptom, all connections to the somatic symptom domain and vice versa), the weights of these connections were summed for all symptoms [244]. In addition, we examined whether neurovegetative and cognitive/affective MDD/GAD symptoms differed with respect to their connectivity to the somatic domain by calculating their mean summed weight of associations to the somatic domain. To test whether these means differed significantly, we used a permutation test described in [236] that compares the observed difference to a distribution of possible differences between the groups of

symptoms. To create this distribution, MDD/GAD symptoms were assigned randomly to two groups 100,000 times, and each time the groups were compared by calculating the difference in their mean strength of associations to the somatic domain. If the observed difference between neurovegetative and cognitive/affective symptoms was within the 2.5% on either side of this distribution (i.e., $p \leq .05$), it was considered significant.

Sensitivity analyses

For our main analyses, we had dichotomized all items as the assumption of normality was not satisfied in our data. This, however, naturally results in a loss of information on the frequency and/or severity of symptoms. We examined whether dichotomization had influenced our conclusions by estimating the network structure of the non-dichotomized MDD/GAD and somatic symptoms with partial correlations using qgraph [241]. Similar to eLasso (for the dichotomized symptoms), an l_1 -penalty [239] and the extended Bayesian Information Criterion [240] were used.

RESULTS

Sample characteristics

Mean age of the sample was 41.7 (SD=13.1) years, 66.1% of participants were women, and participants received education for an average period of 12.2 (SD=3.2) years (see **Table 1**). **Supplementary Table 2** shows that prevalence rates of MDD/GAD symptoms varied from 26.7% (psychomotor retardation) to 79.5% (insomnia), while rates for somatic symptoms ranged between 3.3% (fainting) and 64.8% (muscle pain).

Table 1. Sample characteristics (N=2,704).

	N (%) / mean (SD) ^a
Sociodemographics	
Age in years	41.7 (13.1)
Female	1787 (66.1%)
Education in years	12.2 (3.2)
Psychiatric disorders	
MDD in past month	697 (25.8%)
GAD in past month	344 (12.7%)
Other depressive and/or anxiety disorder in past month	929 (34.4%)

^a Based on descriptive statistics.

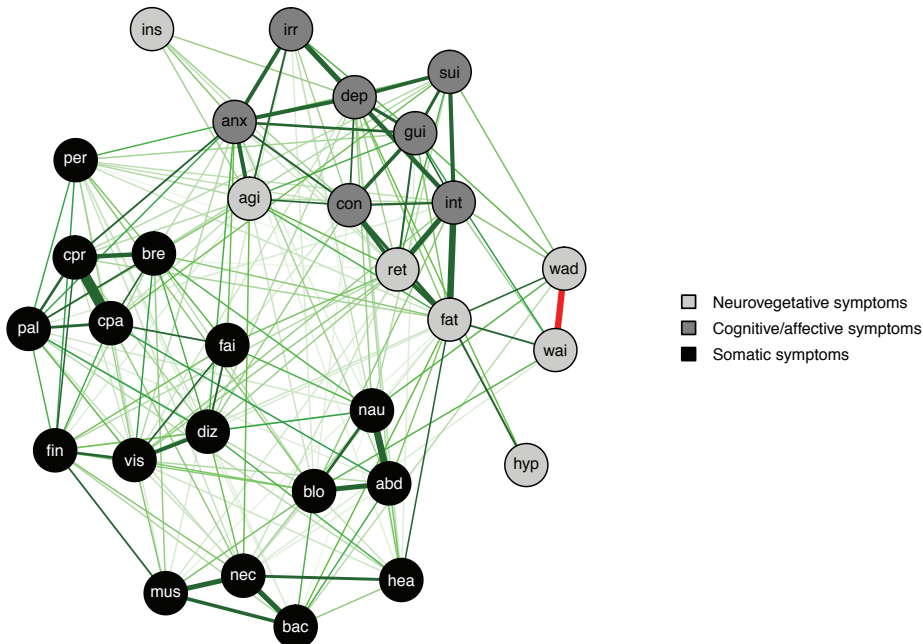
The general network structure of MDD/GAD and somatic symptoms

The estimated network structure of MDD/GAD and somatic symptoms is presented in **Figure 1** (for connection weights see **Supplementary Table 3**). All symptoms were directly or indirectly associated and the network had a high density (i.e., 44.1% of potential connections were observed in the network), indicating that the symptoms were highly connected. All connections were positive, except for the association between weight/appetite increase [wai] and weight/appetite decrease [wad]. Symptoms tended to form two clusters of highly connected MDD/GAD symptoms (the grey symptoms in Figure 1) and somatic symptoms (the black symptoms, Figure 1). In the MDD/GAD domain, neurovegetative and cognitive/affective symptoms were strongly interconnected, although the neurovegetative symptoms referring to weight/appetite change and sleep change had more peripheral positions. Between the MDD/GAD domain and somatic domain, numerous associations were observed.

Connections between MDD/GAD symptoms and somatic symptoms

To unravel the co-occurrence of MDD/GAD with somatic symptoms, we focused on associations between the MDD/GAD domain and the somatic domain. Neurovegetative symptoms were as strongly connected to somatic symptoms as cognitive/affective symptoms (mean $b=0.75$ versus mean $b=0.65$, $p=0.77$). Individual MDD/GAD symptoms, however, varied widely in their strength of associations to the somatic domain (see **Figure 2A**); that is, some symptoms showed strong and multiple connections, while others were not connected to any somatic symptom. The MDD/GAD symptom with the highest summed weight of connections to somatic symptoms ($b=2.35$) was the cognitive/affective symptom anxiety [anx]. It showed 10 connections, of which the associations with pressure/tight feeling in chest [cpr] ($b=0.50$) and palpitations [pal] ($b=0.38$) were the strongest. Next, the neurovegetative symptom fatigue [fat] had the highest summed weight of connections to somatic symptoms ($b=1.65$). Of its 10 connections, the associations with headache [hea] ($b=0.43$) and back pain [bac] ($b=0.28$) were the strongest. In contrast, the neurovegetative symptoms hypersomnia [hyp] and insomnia [ins] were not connected to any somatic symptom.

Figure 1. The network structure of neurovegetative and cognitive/affective symptoms of MDD/GAD and somatic symptoms.



Symptoms are represented by nodes (color refers to type of symptom), and their associations by edges (green = positive association, red = negative association). Thicker edges represent stronger associations.

Neurovegetative symptoms

agi	Psychomotor agitation
fat	Fatigue
hyp	Hypersomnia
ins	Insomnia
ret	Psychomotor retardation
wai	Weight/appetite increase
wad	Weight/appetite decrease

Cognitive/affective symptoms

anx	Anxiety
con	Concentration problems
dep	Depressed mood
gui	Guilt/worthlessness
irr	Irritable
int	Loss of interest/pleasure
sui	Suicidality

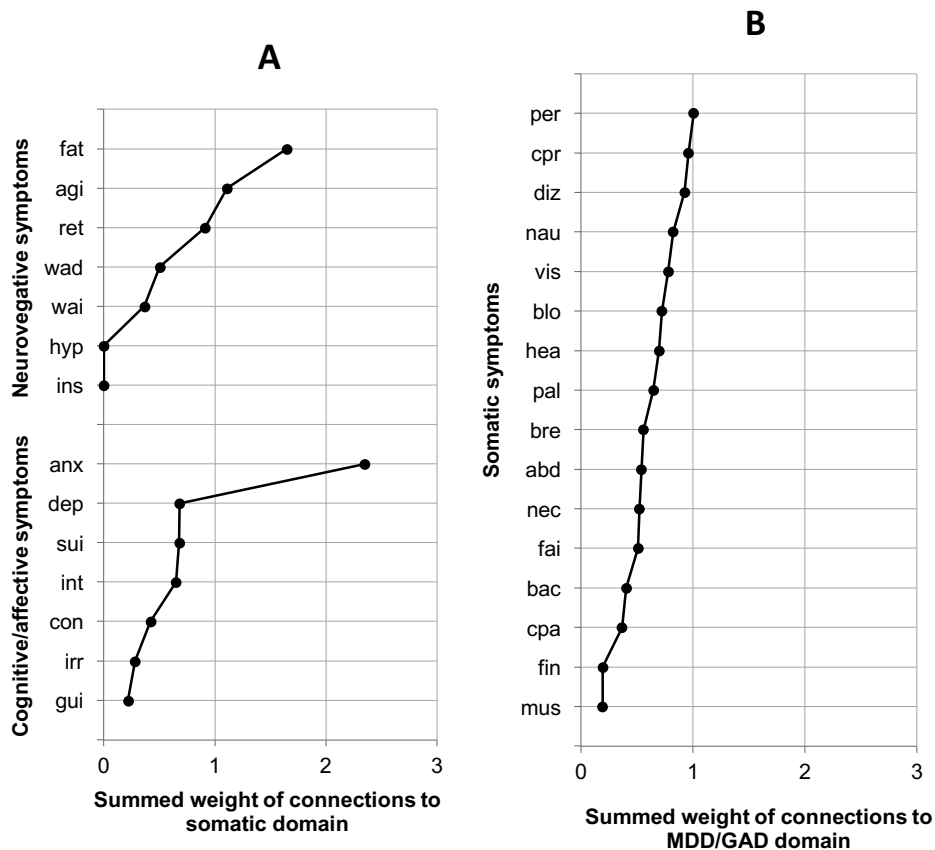
Somatic symptoms

abd	Abdominal pain
bac	Back pain
blo	Bloated feeling in abdomen/stomach area
bre	Shortness of breath
cpa	Chest pain
cpr	Pressure/tight feeling in chest
diz	Dizziness/feeling lightheaded
fai	Fainting
fin	Tingling in fingers
hea	Headache
mus	Muscle pain
nau	Nausea
nec	Neck pain
pal	Palpitations
per	Excessive perspiration
vis	Blurred vision/spots in front of eyes

Similarly, individual somatic symptoms differed substantially in their associations with MDD/GAD symptoms (see **Figure 2B**). The somatic symptom with the highest summed weight of connections to MDD/GAD symptoms ($b=1.00$) was excessive perspiration [per].

This symptom showed 7 associations, of which the strongest were with anxiety [anx] ($b=0.34$), guilt/worthlessness [gui] ($b=0.16$), and psychomotor agitation [agi] ($b=0.14$). Pressure/tight feeling in chest [cpr] was also strongly related to MDD/GAD symptoms as it showed 5 connections with a summed weight of $b=0.96$. Its strongest connection was to anxiety [anx] ($b=0.50$). Interestingly, all somatic symptoms were related to the MDD/GAD symptom domain, but some somatic symptoms showed only weak associations. Muscle pain, for example, showed 3 weak connections with a summed weight of $b=0.19$ to loss of interest/pleasure [int] ($b=0.08$), irritable [irr] ($b=0.07$), and fatigue [fat] ($b=0.04$). Tingling in fingers [fin] was also weakly associated with MDD/GAD symptoms (summed weight of connections $b=0.19$) as it was only connected to psychomotor retardation [ret] ($b=0.14$) and psychomotor agitation [agi] ($b=0.06$).

Figure 2. The summed weight of all connections from specific symptoms to the opposite symptom domain.



A: Summed weight of connections from MDD/GAD symptoms to the somatic symptom domain; B: Summed weight of connections from somatic symptoms to the MDD/GAD symptom domain. Symptoms are ordered based on the strength of their connections.

Sensitivity analyses

Finally, we performed a set of sensitivity analyses to examine if the dichotomization of our data had affected the network structure. **Supplementary Figure 1** shows the network structure of the polytomous MDD, GAD, and somatic symptoms. The network had a somewhat higher density than the network based on the dichotomized items (53.8% versus 44.1%), but the general structure was similar. In addition, although some variation was observed in the strength of individual symptoms to the opposite symptom domain compared to the network of dichotomized items (e.g., polytomous insomnia was moderately associated with somatic symptoms whereas dichotomized insomnia was not), the patterns of associations to the other symptom domain were comparable. That is, anxiety [anx] and fatigue [fat] showed the strongest associations to the somatic domain, and excessive perspiration [per] and pressure/tight feeling in chest [cpr] were among the somatic symptoms with the strongest associations to the MDD/GAD domain.

DISCUSSION

This study presented the complex network structure of individual MDD/GAD symptoms and individual somatic symptoms. In contrast to our hypothesis, neurovegetative symptoms of MDD/GAD did not differ with respect to their strength of associations to somatic symptoms from cognitive/affective symptoms of MDD/GAD. In addition, specific MDD/GAD symptoms such as anxiety and fatigue showed strong associations whereas hypersomnia and insomnia were not connected to the somatic domain at all. Somatic symptoms with many and/or strong connections to MDD/GAD symptoms included excessive perspiration and pressure/tight feeling in chest, while muscle pain and tingling in fingers showed limited and weak associations.

This exploratory study is the first in applying a network estimation technique to data on MDD/GAD and somatic symptomatology, which enabled us to provide insight into the unique contributions of individual symptoms in this co-occurrence. Another strength of this study is the use of the recently developed method eLasso to infer the network structure from the observed data, since this technique is not based on often untenable assumptions about psychopathology such as linearity and normality [238]. In addition, the technique does not rely on arbitrary cut-offs to determine the presence of connections in the network, as opposed to other network estimation techniques based on correlation or partial correlation [238]. Third, this study included a large sample (N=2,704) of persons with and without depressive and/or anxiety disorders, which ensured variability in symptom ratings and, consequently, prevented the network estimation to suffer from floor and ceiling effects.

Several limitations should also be discussed. First, MDD/GAD symptoms were assessed with the IDS, whereas somatic symptoms were assessed with the 4DSQ. Since these questionnaires had varying response categories, this might have impacted the empirical network structure of symptoms; that is, clustering of symptoms may have occurred based on these questionnaires. However, we recoded all items into either absent (the first response category in all instruments) or present (combining all other response categories) to create comparable response categories across instruments. In addition, although most DSM-IV criteria of MDD/GAD were included in the IDS, two criteria of GAD (i.e., criterion B: difficulty controlling worry and C5: muscle tension) were not assessed. Third, the network estimation technique eLasso has high specificity but moderate sensitivity [238]. This implies that the reported connections are most probably correct, but some weak connections in reality might have been missed. Fourth, the NESDA study mainly recruited participants with a lifetime DSM diagnosis of a depressive and/or anxiety disorder (2,081 of the 2,704 participants in our sample), who were selected for participation if they reported multiple DSM symptoms. Participants in our sample therefore probably had a higher number of DSM symptoms than persons from the general population, which could have led to stronger associations among these symptoms in our network structure. Generalization of our results may also be impaired as 9.3% of participants of the original NESDA study were excluded due to missing data, leading to a younger, higher educated sample with better mental health.

The classes of neurovegetative symptoms and cognitive/affective symptoms showed similar strengths of associations to somatic symptoms. This is in line with a study by Fried et al. [236] reporting that the most central symptoms in a network structure of depressive, anxiety, and some somatic symptoms included both neurovegetative and cognitive/affective symptoms. This indicates that these symptoms are equally important in their co-occurrence with somatic symptomatology and, therefore, highlights the importance of considering neurovegetative as well as cognitive/affective symptoms in persons with somatic symptoms. Additionally, these findings suggest that the strict mind-body dichotomy proposed in previous research might not apply for MDD/GAD symptoms [245,246], which was supported by the strong clustering of these symptoms in the network structure. Rather, the symptoms may be conceptualized as a dynamic system of related symptoms. A recent study [247], for example, demonstrated that neurovegetative and cognitive/affective depressive symptoms were intimately connected through patterns of temporal influence.

In addition, individual symptoms of MDD/GAD as well as somatic symptoms differed considerably in the number and the strength of their associations in the network and, as a result, the MDD/GAD domain and somatic domain were connected via specific symptom pairs. This corroborates findings of an earlier study reporting that individual symptoms

of depression and anxiety were associated with unique sets of somatic symptoms and vice versa [232]. Similar to our results, anxiety symptoms were more strongly related to somatic symptoms than symptoms such as guilt and suicidal ideation, and dizziness showed more connections to depressive and anxiety symptoms than symptoms like nausea and headache [232]. These findings imply that studying the co-occurrence of these symptom domains by using sum scores obfuscates important differences in the patterns of associations shown by specific symptoms [69]. Consequently, they stress the relevance of an approach focusing on individual symptoms and their connections. Concentrating on individual symptoms is especially important as the connectivity of symptoms in a network may have important implications for prognosis. A recent study, for example, showed that MDD symptoms with a higher connectivity in a similar cross-sectional network more strongly predicted the onset of a full-blown MDD during six years of follow-up than MDD symptoms with a lower connectivity [237]. This indicates that bridging MDD/GAD and somatic symptoms, which show strong connections to the other symptom domain, may be more central in the mechanisms leading to and/or maintaining the co-occurrence of MDD/GAD and somatic symptomatology than non-bridging symptoms [84]. Consequently, a decrease of a bridging symptom is likely to result in a deactivation of symptoms of the other symptom domain in the network, whereas change in a non-bridging symptom may have little effect on these symptoms. Hence, it could be valuable to target prevention and intervention strategies specifically to the bridging symptoms in our network.

As the network approach focuses on specific associations between individual symptoms, it could also help to formulate hypotheses regarding the mechanisms behind the association of MDD/GAD with somatic symptomatology. For instance, some associations in the network structure might be causal (e.g., weight/appetite increase → bloated feeling abdomen; dizziness → concentration problems), whereas common causes may underlie others (e.g., HPA-axis disturbances could explain the strong associations of anxiety and psychomotor agitation with cardiopulmonary symptoms [248,249]). Although these suggestions are speculative, they indicate that different mechanisms may underlie associations between specific symptom pairs in the network. Longitudinal data from ecological momentary assessments that record individual symptoms repeatedly over time might aid in unraveling the dynamic relations between MDD/GAD and somatic symptoms. The general structure of the network is also of relevance for the ongoing discussion on the validity of the current classification of MDD/GAD and somatic symptomatology in the DSM. First, in line with other studies [74,250], we found that symptoms of MDD and symptoms of GAD formed one cluster in the network. This raises the question whether symptoms of MDD and GAD should be conceptualized as expressions of separate disorders, which was addressed in the DSM-5 by adding an anxiety distress specifier

to the diagnosis of MDD [16]. In addition, it has repeatedly been argued that somatic symptomatology should be included in the diagnostic criteria of MDD/GAD as they are important features of depressed and anxious states [102,224,251]. Our network, however, showed separate domains of MDD/GAD symptoms and somatic symptoms. This is also in accordance with a factor analysis in patients with a depressive disorder showing that MDD items loaded on other factors than pain symptoms [252] and may imply that somatic symptomatology should not be part of the DSM criteria of MDD/GAD. This study demonstrated the differential associations of individual symptoms in the co-occurrence of MDD/GAD diagnoses and somatic symptomatology. We would like to encourage other researchers to consider the contributions of individual symptoms to this co-occurrence in longitudinal studies and to focus on the bridging symptoms found in this study. In addition, targeting interventions to bridging symptoms may help to improve outcomes of patients with MDD/GAD and/or somatic symptomatology.

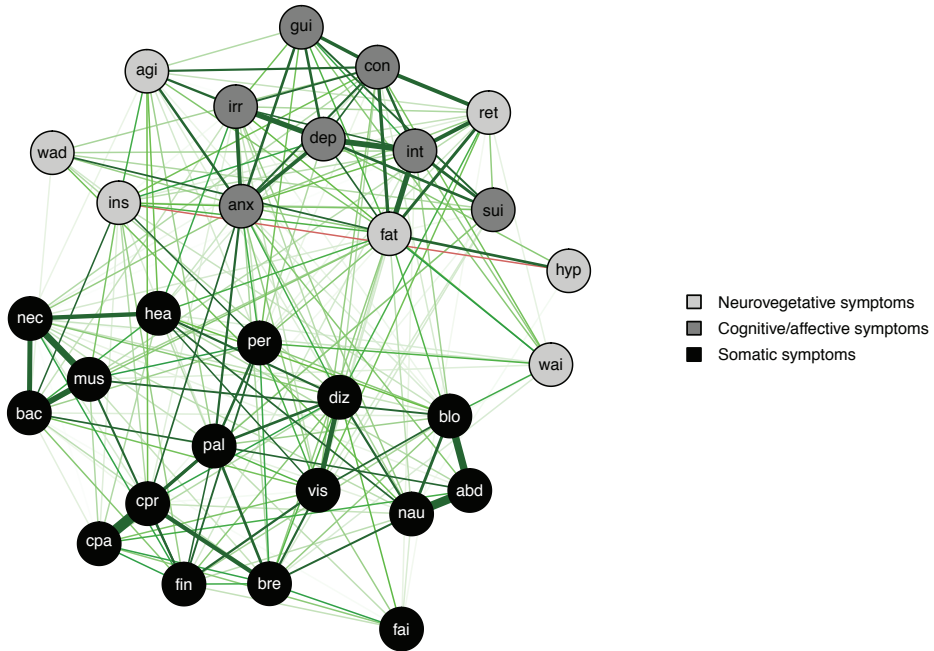
SUPPLEMENTARY MATERIAL**Supplementary Table 1.** Classification of MDD/GAD symptoms.

Symptom	Abbreviation	MDD criterion	GAD criterion	IDS item(s)
<u>Neurovegetative symptoms</u>				
Weight/appetite increase	wai	A3	-	12,14
Weight/appetite decrease	wad	A3	-	11,13
Hypersomnia	hyp	A4	-	4
Insomnia	ins	A4	C6	1,2,3
Psychomotor agitation	agi	A5	C1	24
Psychomotor retardation	ret	A5	-	23
Fatigue	fat	A6	C2	20
<u>Cognitive/affective symptoms</u>				
Depressed mood	dep	A1	-	5
Loss of interest/pleasure	int	A2	-	19,20
Anxiety	anx	-	A	7
Guilt/worthlessness	gui	A7	-	16
Concentration problems	con	A8	C3	15
Suicidality	sui	A9	-	18
Irritable	irr	-	C4	6

Supplementary Table 2. Symptom prevalence.

Symptom	Prevalence N (%)
<u>MDD/GAD symptoms</u>	
<i>Neurovegetative symptoms</i>	
Fatigue	1537 (56.8%)
Hypersomnia	991 (36.6%)
Insomnia	2151 (79.5%)
Psychomotor agitation	1201 (44.4%)
Psychomotor retardation	723 (26.7%)
Weight/appetite increase	950 (35.1%)
Weight/appetite decrease	860 (31.8%)
<i>Cognitive/affective symptoms</i>	
Anxiety	1699 (62.8%)
Concentration problems	1589 (58.8%)
Depressed mood	1558 (57.6%)
Guilt/worthlessness	1252 (46.3%)
Irritable	1713 (63.4%)
Loss of interest/pleasure	1307 (48.3%)
Suicidality	736 (27.2%)
<u>Somatic symptoms</u>	
Abdominal pain	1074 (39.7%)
Back pain	1685 (62.3%)
Bloated feeling in abdomen/stomach area	1404 (51.9%)
Blurred vision/spots in front of eyes	1128 (41.7%)
Chest pain	593 (21.9%)
Dizziness/feeling lightheaded	1424 (52.7%)
Excessive perspiration	1342 (49.6%)
Fainting	89 (3.3%)
Headache	1697 (62.8%)
Muscle pain	1753 (64.8%)
Neck pain	1498 (55.4%)
Nausea	1154 (42.7%)
Palpitations	1138 (42.1%)
Pressure/tight feeling in chest	942 (34.8%)
Shortness of breath	903 (33.4%)
Tingling in fingers	875 (32.4%)

Supplementary Figure 1. The network structure of neurovegetative and cognitive/affective symptoms of MDD/GAD and somatic symptoms based on polytomous items.



Symptoms are represented by nodes (color refers to type of symptom), and their associations by edges (green = positive association, red = negative association). Thicker edges represent stronger associations.

