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

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Background. 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 and more insight into their relationships 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.

Method. MDD/GAD symptoms were assessed in 2704 participants (mean age 41.7 years, 66.1% female) from the Netherlands Study of Depression and Anxiety using the Inventory of Depressive Symptomatology. Somatic symptoms were assessed with the somatization scale of the Four-Dimensional Symptom Questionnaire. 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.

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Key words: Co-morbidity, generalized anxiety disorder, major depressive disorder, network analyses, somatic symptoms.

Introduction

Major depressive disorder (MDD) and generalized anxiety disorder (GAD) are prevalent and debilitating (Kessler *et al.* 2005; Wittchen *et al.* 2011). The conditions are strongly connected, as their symptoms frequently co-occur and show strong overlap (American Psychiatric Association, 1994; Cramer *et al.* 2010). Consequently, comorbidity rates between the disorders have been reported to be as high as 40–60% (Hettema, 2008).

Previous studies have shown that MDD and GAD are associated with higher levels of somatic

symptomatology (Henningsen *et al.* 2003; Haug *et al.* 2004; Rosmalen *et al.* 2011; Bekhuis *et al.* 2015). 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 (Bekhuis *et al.* 2015). 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 (Borsboom & Cramer, 2013) 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

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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 headache and vice versa) (Uhlrig *et al.* 2014). Cognitive/affective symptoms, however, are more strongly related to mental processes (Lux & Kendler, 2010) and, consequently, could show only weak connections to somatic symptomatology (Wesley *et al.* 1991). 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 (Borsboom & Cramer, 2013). 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 (Cramer *et al.* 2010). In a recent study, for example, Boschloo *et al.* (2016a) presented the network structure of emotional and behavioural 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.* (2016a) did not include Diagnostic and Statistical Manual of Mental Disorders (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 relationships between individual MDD/GAD symptoms and somatic

symptoms in a large sample ($n=2704$) 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.

Method

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 2981 participants were included for the baseline assessment in 2004–2007, consisting of 652 (22%) healthy controls with no lifetime depressive and/or anxiety disorder, 1411 (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; Wittchen *et al.* 1991]. 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; Kessler *et al.* 2002; and the short-form CIDI by telephone) conducted among a random sample of consulting patients of 65 general practitioners. Mental health care participants were recruited consecutively when newly enrolled at one 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 (Penninx *et al.* 2008).

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 2704 persons. Participants with complete data were younger [41.7 (s.d. = 13.1) *v.* 43.5 (s.d. = 12.6) years, $p =$

0.03], received education for a longer period [12.2 (s.d. = 3.2) *v.* 11.5 (s.d. = 3.5) years of education, $p = 0.001$] and were less likely to have past-month MDD (25.8% *v.* 37.9%, $p < 0.001$) or GAD (12.7% *v.* 19.1%, $p = 0.004$), but did not differ with respect to gender (66.1% *v.* 69.3% female, $p = 0.29$) from participants with missing data.

DSM, fourth edition (DSM-IV) symptoms of MDD/GAD

The frequency/severity of 14 DSM-IV MDD and/or GAD symptoms (American Psychiatric Association, 1994) during the past week was assessed with the Inventory of Depressive Symptomatology self-report version (IDS-SR₃₀; Rush *et al.* 1986, 1996). As in prior studies (van Borkulo *et al.* 2015; Boschloo *et al.* 2016b; Fried *et al.* 2016), 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 (Boschloo *et al.* 2016b; Fried *et al.* 2016). Based on dimensions identified in previous studies (Wardenaar *et al.* 2010; Duvis *et al.* 2013), 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 online Supplementary Table S1.

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; Terluin *et al.* 2006). 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 ‘IsingFit’ in R; van Borkulo *et al.* 2014) was used. eLasso uses *l1*-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 *l1*-penalty is imposed on the regression coefficients to identify models with an optimal balance between parsimony and goodness of fit (Tibshirani, 1996). To find the best-fitting model, the extended Bayesian information criterion is used to assess goodness of fit (Chen & Chen, 2008). 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 (van Borkulo *et al.* 2014).

Based on the estimated symptom associations, a weighted, undirected graph was visualized using the package ‘qgraph’ (Epskamp *et al.* 2012) in R. In a network structure, nodes (circles) represent symptoms and edges (lines) represent associations between symptoms. Solid edges indicate positive associations and dotted edges represent negative associations (online: green edges indicate positive associations and red edges represent negative associations). The thickness of lines 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 (Fruchterman & Reingold, 1991).

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 (Kolaczyk, 2009). 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 (Barrat *et al.* 2004). 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 Fried *et al.* (2016) that compares the observed difference with 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. $p \leq 0.05$), 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 (Epskamp *et al.* 2012). Similar to eLasso (for the dichotomized symptoms), an l_1 -penalty (Tibshirani, 1996) and the extended Bayesian information criterion (Chen & Chen, 2008) were used.

Results

Sample characteristics

The mean age of the sample was 41.7 (s.d. = 13.1) years, 66.1% of participants were women, and participants received education for an average period of 12.2 (s.d. = 3.2) years (see Table 1). Online Supplementary Table S2 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).

General network structure of MDD/GAD and somatic symptoms

The estimated network structure of MDD/GAD and somatic symptoms is presented in Fig. 1 (for connection weights, see online Supplementary Table S3). 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

Table 1. Sample characteristics ($n = 2704$)

	<i>n</i> (%) or mean (s.d.) ^a
Sociodemographics	
Mean age, years (s.d.)	41.7 (13.1)
Female, <i>n</i> (%)	1787 (66.1)
Mean duration of education, years (s.d.)	12.2 (3.2)
Psychiatric disorders, <i>n</i> (%)	
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)
Functional somatic syndromes, <i>n</i> (%)	
Chronic fatigue syndrome	41 (1.5)
Fibromyalgia	56 (2.1)
Irritable bowel syndrome	220 (8.1)

s.d., Standard deviation; MDD, major depressive disorder; GAD, generalized anxiety disorder.

^aBased on descriptive statistics.

symptoms, Fig. 1) and somatic symptoms (the black symptoms, Fig. 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 $b = 0.75$ *v.* mean $b = 0.65$, $p = 0.77$). Individual MDD/GAD symptoms, however, varied widely in their strength of associations to the somatic domain (see Fig. 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 association 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 association with

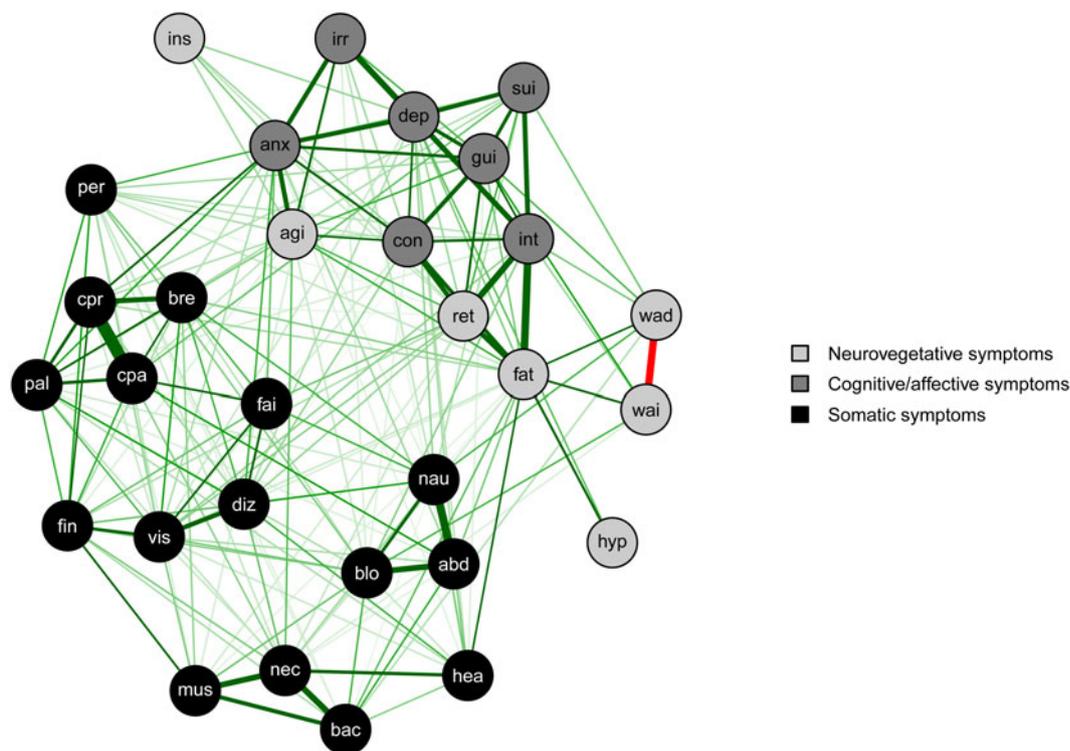


Fig. 1. Network structure of neurovegetative and cognitive/affective symptoms of major depressive disorder/generalized anxiety disorder and somatic symptoms. Symptoms are represented by nodes (shading refers to type of symptom) and their associations by edges (lines) (solid line = positive association, dotted line = negative association; online: green = positive association, red = negative association). Thicker edges represent stronger associations. ins, Insomnia; irr, irritable; anx, anxiety; dep, depressed mood; sui, suicidality; gui, guilt/worthlessness; agi, psychomotor agitation; con, concentration problems; int, loss of interest/pleasure; ret, psychomotor retardation; fat, fatigue; wad, weight/appetite decrease; wai, weight/appetite increase; hyp, hypersomnia; per, excessive perspiration; cpr, pressure/tight feeling in chest; bre, shortness of breath; pal, palpitations; cpa, chest pain; fai, fainting; diz, dizziness/feeling lightheaded; vis, blurred vision/spots in front of eyes; fin, tingling in fingers; nau, nausea; blo, bloated feeling in abdomen/stomach area; abd, abdominal pain; hea, headache; mus, muscle pain; nec, neck pain; bac, back pain. For the colour figure, see the online version of the paper.

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.

Similarly, individual somatic symptoms differed substantially in their associations with MDD/GAD symptoms (see Fig. 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 seven 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 five 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 three 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) ($b=0.06$).

Sensitivity analyses

Finally, we performed a set of sensitivity analyses to examine if the dichotomization of our data had affected the network structure. Online Supplementary Fig. S1 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% *v.* 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

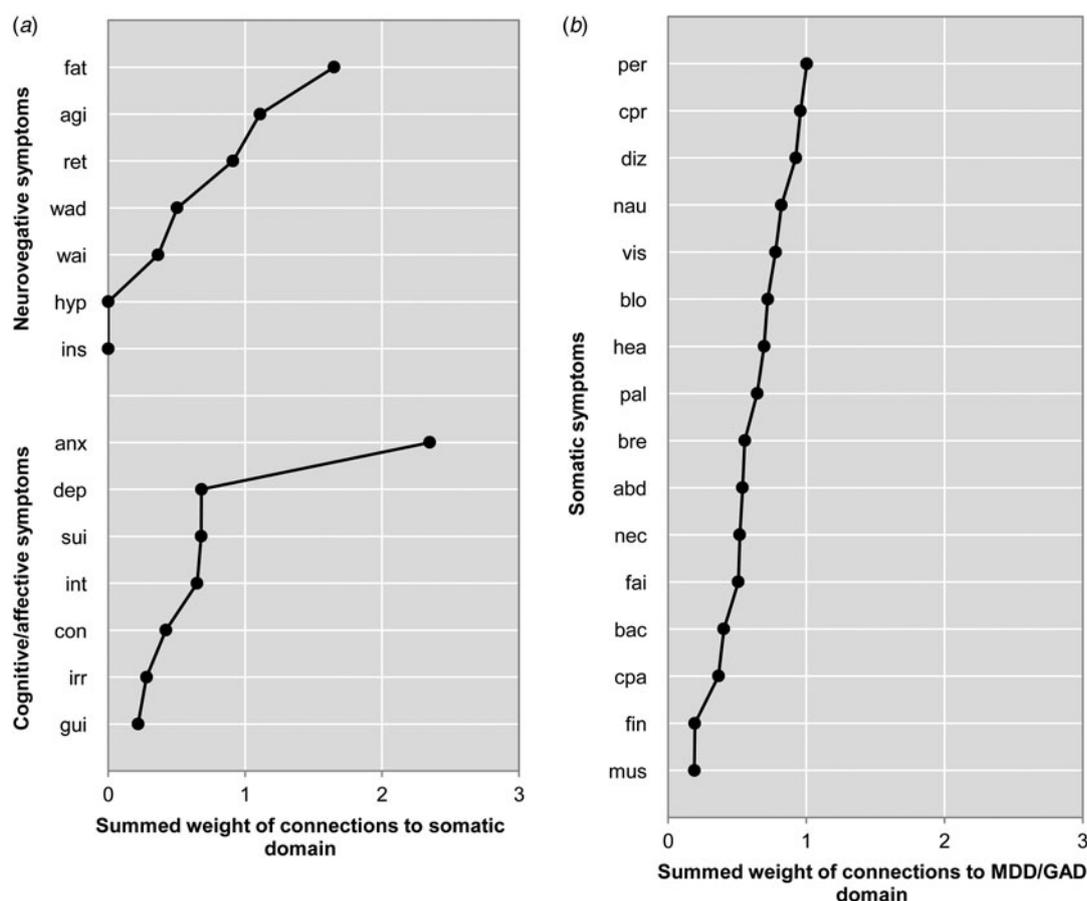


Fig. 2. Summed weight of all connections from specific symptoms to the opposite symptom domain. (a) Summed weight of connections from major depressive disorder/generalized anxiety disorder (MDD/GAD) symptoms to the somatic symptom domain. (b) Summed weight of connections from somatic symptoms to the MDD/GAD symptom domain. Symptoms are ordered based on the strength of their connections. fat, Fatigue; agi, psychomotor agitation; ret, psychomotor retardation; wad, weight/appetite decrease; wai, weight/appetite increase; hyp, hypersomnia; ins, insomnia; anx, anxiety; dep, depressed mood; sui, suicidality; int, loss of interest/pleasure; con, concentration problems; irr, irritable; gui, guilt/worthlessness; per, excessive perspiration; cpr, pressure/tight feeling in chest; diz, dizziness/feeling lightheaded; nau, nausea; vis, blurred vision/spots in front of eyes; blo, bloated feeling in abdomen/stomach area; hea, headache; pal, palpitations; bre, shortness of breath; abd, abdominal pain; nec, neck pain; fai, fainting; bac, back pain; cpa, chest pain; fin, tingling in fingers; mus, muscle pain.

with the network of dichotomized items (e.g. polytomous insomnia was moderately associated with somatic symptoms whereas dichotomized insomnia was not), the patterns of associations with the other symptoms domain were comparable. That is, anxiety (anx) and fatigue (fat) showed the strongest associations with the somatic domain, and excessive perspiration (per) and pressure/tight feeling in chest (cpr) were among the somatic symptoms with the strongest associations with 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 (van Borkulo *et al.* 2014). 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 (van Borkulo *et al.* 2014). Third, this study included a large sample ($n=2704$) 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 made an impact on 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 (van Borkulo *et al.* 2014). This implies that the reported connections are most probably correct, but some weak connections in reality might have been missed. Fourth, the NESDA mainly recruited participants with a lifetime DSM diagnosis of a depressive and/or anxiety disorder (2081 of the 2704 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 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 with somatic symptoms. This is in line with a study by Fried *et al.* (2016) 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 (Whisman *et al.* 2000; Manian *et al.* 2013), 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 (Bringmann *et al.* 2015), 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 (Boschloo *et al.* 2016a). 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 (Boschloo *et al.* 2016a). These findings imply that studying the co-occurrence of these symptom domains by using sum scores obscures important differences in the patterns of associations shown by specific symptoms (Fried & Nesse, 2015). 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 6 years of follow-up than MDD symptoms with a lower connectivity (Boschloo *et al.* 2016b). 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 (Borsboom & Cramer, 2013). Consequently, a decrease of a bridging symptom is likely to result in a deactivation of symptoms of the other symptom domain, 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 in abdomen; dizziness → concentration problems), whereas common causes may underlie others (e.g. hypothalamic–pituitary–adrenal axis disturbances could explain the strong associations of anxiety and psychomotor agitation with cardiopulmonary symptoms; Smith & Vale, 2006; Abelson *et al.* 2007). 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 relationships 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 (Krueger, 1999; Cramer *et al.* 2010), 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 (American Psychiatric Association, 2013). 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 (Fava, 2002; Kapfhammer, 2006; Chakraborty *et al.* 2012). Our network, however, showed separate domains of MDD/GAD symptoms and somatic symptoms. This is also in accordance with a factor analysis in depressed patients showing that MDD items loaded on other factors than pain symptoms (Hong *et al.* 2015) 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

The supplementary material for this article can be found at <http://dx.doi.org/10.1017/S0033291716001550>

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