Symptom network models in depression research

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CHAPTER 8

A PROSPECTIVE STUDY ON HOW SYMPTOMS IN A NETWORK PREDICT THE ONSET OF DEPRESSION

Adapted from:

Boschloo, L., **Van Borkulo, C. D.**, Borsboom, D., & Schoevers, R.A. (2016). A Prospective Study on How Symptoms in a Network Predict the Onset of Depression. *Psychotherapy and Psychosomatics, 85*, 183-184.

To explain the overt heterogeneous nature of major depressive disorder (MDD), it could be valuable to focus on individual symptoms (Fried, Boschloo, et al., 2015). Recent research, for example, showed that MDD symptoms differ in their underlying biology, risk factors and psychosocial impairments (for a review, see Fried & Nesse, 2015b). In addition, the presence of specific symptoms (e.g., psychomotor agitation) may have important clinical implications, such as expectations regarding the response to antidepressants (Sani et al., 2014).

8.1 The network approach

The network approach is a conceptualization that specifically focuses on individual symptoms (Borsboom & Cramer, 2013). According to this approach, psychopathology results from the associations between symptoms, and each of these symptoms may have its unique set of associations with other symptoms. This information can be visualized into a network, in which symptoms are represented as nodes and the associations between them as lines.

In a recent study, we estimated the network of a large set of psychiatric symptoms, including those of MDD, and indeed found that symptoms differed in the number and strength of associations (Boschloo et al., 2015). For example, depressed mood and fatigue were *central* in the network (i.e., having many and/or strong associations), whereas a decrease and increase in weight/appetite were not. Central symptoms are believed to have considerable impact on other symptoms and, consequently, more strongly predict the onset of MDD than symptoms that are less central.

8.2 Aim of this study

The present study aimed to test whether symptom centrality was indeed related to the risk of developing MDD. Therefore, we selected 501 adults with no lifetime DSM-IV depressive or anxiety disorder from the baseline assessment of the Netherlands Study of Depression and Anxiety (NESDA; for a detailed description of the study design, see Penninx et al., 2008). ℓ_1-regularized partial correlations were used to compute a sparse network of the 12 MDD symptoms as assessed with specific items of the Inventory of Depressive Symptomatology (for a detailed description of the procedures, see Van Borkulo et al., 2015). To determine the cen-

trality of each of the symptoms in the network, *symptom strength* was calculated as the sum of all direct correlations with other symptoms.

8.3 Results

Figure 8.1 shows the resulting network of baseline MDD symptoms. Symptoms differed substantially in both the number and magnitude of associations, but, overall, symptom strength was the highest for fatigue, concentration problems, loss of interest/pleasure and depressed mood. In contrast, hypersomnia, suicidal thoughts and a decrease in weight/appetite had the lowest symptom strength.

In this sample of healthy controls, we identified those who developed a DSM-IV MDD at the 2-, 4-, or 6-year follow-up assessment ($n = 79$) and those who did not ($n = 422$). Table 8.1 displays the results from univariable logistic regression analyses which showed that loss of interest/pleasure, depressed mood, fatigue and concentration problems (i.e., those symptoms with the highest symptom strength in the baseline network) were the strongest predictors (all odds ratios $OR \geq 3.02$), whereas suicidal thoughts, hypersomnia and a decrease in weight/appetite (i.e., those symptoms with the lowest symptom strength in the baseline network) were not or only weakly related to the onset of MDD (all $OR \leq 1.75$). In general, symptoms that were central in the baseline network more strongly predicted the onset of MDD than symptoms that were less central (see Figure 8.2; $r = 0.87$, $p < 0.001$).

Then, we tested whether information on the centrality of symptoms could improve the prediction of the onset of MDD. In addition to a conventional severity measure based on the sum of the 12 MDD symptoms (i.e., the unweighted severity measure), a new severity measure was calculated in which the 12 MDD symptoms were weighted for symptom strength (i.e., the weighted severity measure). Multivariable logistic regression analyses showed that the weighted severity measure more strongly predicted the onset of MDD than the unweighted measure (adjusted $OR = 1.66$, $p = 0.043$ vs. adjusted $OR = 1.00$, $p = 0.995$).

8.4 Conclusion

Our findings indicate that the risk of developing MDD depends on the type of subthreshold symptom that a person reports. Loss of interest/pleasure, depressed

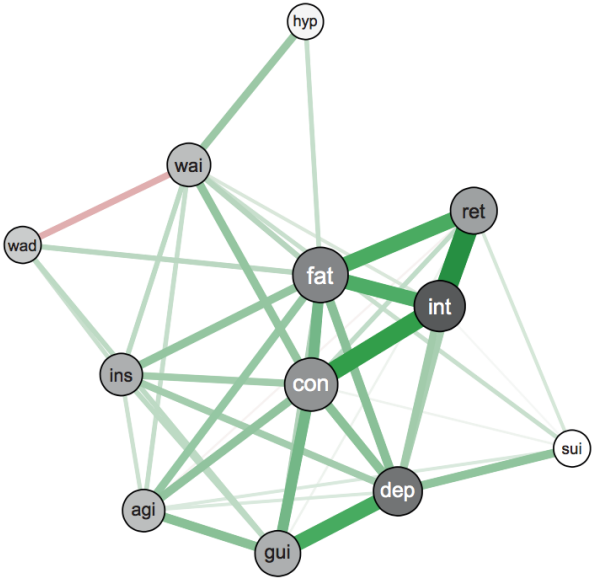

FIGURE 8.1. Baseline MDD symptom network in persons with no life-time depressive or anxiety disorder (n = 501). All lines represent positive correlations, except for the line between 'wad' and 'wai', which represents a negative correlation. Thicker lines represent stronger correlations. Larger nodes represent symptoms with a higher symptom strength and darker nodes represent symptoms with stronger associations with the onset of MDD during the 6 years of follow-up. Abbreviations: dep - depressed mood; int - loss of interest/pleasure; wad - decrease in weight/appetite; wai - increase in weight/appetite; ins - insomnia; hyp - hypersomnia; ret - psychomotor retardation; agi - psychomotor retardation; fat - fatigue; gui - feelings of guilt/worthlessness; con - concentration problems; sui - suicidal thougths.

TABLE 8.1. Results from univariable logistic regression.

	Description	Centrality of symptom in the network	Association of symptom with the onset of MDD	
		symptom strength	OR	p
dep	depressed mood	0.77	3.68	<0.001
int	loss of interest/pleasure	0.83	4.30	<0.001
wad	decrease in weight/appetite	0.22	1.75	0.030
wai	increase in weight/appetite	0.48	2.06	0.001
ins	insomnia	0.44	2.43	<0.001
hyp	hypersomnia	0.13	1.18	0.456
ret	psychomotor retardation	0.65	2.66	<0.001
agi	psychomotor agitation	0.44	2.09	<0.001
fat	fatigue	1.04	3.34	<0.001
gui	feelings of guilt/worthlessness	0.62	2.36	<0.001
con	concentration problems	0.95	3.02	<0.001
sui	suicidal thoughts	0.21	1.04	0.903

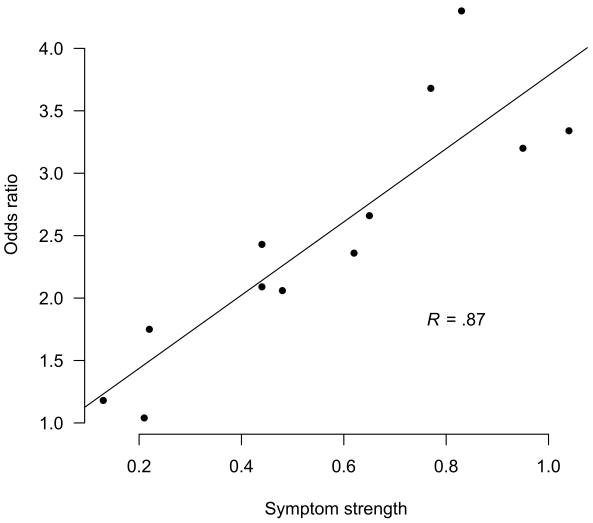

FIGURE 8.2. Scatterplot of symptom strength and odds ratio (R= .87).

mood, fatigue and concentration problems were the most important risk factors, and these symptoms could, therefore, help clinicians (e.g., general practitioners) in identifying persons who are most vulnerable for MDD. These specific symptoms were also central in the MDD symptom network and may, consequently, be valuable targets in prevention strategies. By eliminating or reducing such a central symptom, it is hypothesized that activity within the whole network can be reduced (or prevented). For example, a strategy that encourages a person to engage in pleasant activities does not only have the potential to improve (or prevent) a person′s ability to experience pleasure (symptom "loss of interest/pleasure") but, subsequently, also his or her energy level (connected symptoms "fatigue" and "psychomotor retardation") and ability to concentrate (connected symptom "concentration problems"). Although such strategies are already part of regular prevention programs and have proven to be effective (Buntrock et al., 2015), the network approach may offer a more empirical, data-driven basis that enhances even more focused interventions based on the role of specific symptoms within a network.

Strengths of our study were that we included a large sample of persons with no lifetime DSM-IV depressive or anxiety disorder ($n = 501$) and prospectively examined the onset of DSM-IV MDD during a 6-year follow-up. However, a limitation is that MDD symptoms were assessed at a single time point and, therefore, the temporal relationship between symptoms is unknown. Time series analyses of longitudinal data from the experience sampling method could help to unravel the dynamics of symptom networks over time (aan het Rot et al., 2012), which might also be a promising approach for examining therapeutic changes (for an interesting review on this topic, see Hayes, Yasinski, Ben Barnes, & Bockting, 2015).

In conclusion, subthreshold MDD symptoms were differentially associated with the prospective onset of MDD and these findings demonstrate the value of an approach focusing on individual symptoms. The network approach may be such an approach, as we showed that the risk of developing MDD depended on the centrality of a symptom in the network. This centrality may, therefore, inform clinicians on the symptoms that are likely to have the most prognostic impact when adapted by targeted treatment.