Latent variables and the network perspective

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NOTES

1. The National Comorbidity Survey Replication (NCS-R) is a nationally representative household survey of English speakers 18 years and older in the United States (see Kessler et al. 2004). The NCS-R survey schedule is the version of the World Health Organization (WHO) Composite International Diagnostic Interview that is developed for the WHO World Mental Health Survey Initiative (WMH-CIDI; Kessler & Ustun 2004). The interviews were conducted between February 2001 and April 2003. A total of 9,282 respondents participated in Part 1 of the interview (core diagnostic assessment) that we used for this article. The symptoms that participants reported within one disorder all occurred within the same time frame.

2. We did not collapse the six symptoms that overlap between MDD and GAD into three bridging symptoms because the log odds ratios between each pair of overlapping symptoms were not high enough to warrant such a collapse. A probable explanation for this is that some people, for instance, did report concentration problems in the depression section, but were unable to report those same problems in the generalized anxiety section because that section was skipped (e.g., because the respondent did not experience chronic anxiety).

3. It is prudent to note that feedback loops can create considerable methodological difficulties in model fitting, because they lead to models that cannot be recursively estimated. However, given our present state of ignorance concerning the nature of comorbidity, we think it is more useful to construct a theoretical representation that is likely to be faithful to reality, than it is to construct a model based on a list of desirable computational properties.

4. This network is based on the NCS-R questionnaire that mostly contains dichotomous items. However, some of the items were not (e.g., "How many pounds have you gained?"), and we dichotomized those according to the *DSM-IV* diagnostic algorithms. Details of the dichotomization process are provided at: http://www.aojcramer.com.

5. The *odds ratio* is the ratio of the odds of an event (e.g., suffering from loss of interest) occurring in one group (e.g., people who suffer from depressed mood) to the odds of that event occurring in another group (e.g., people not suffering from depressed mood). For cell counts in a 2x2 contingency table, the sample odds ratio equals $n_{11}n_{22}/n_{12}n_{21}$ (see Agresti 2002). Since the odds ratio scales between zero and infinity, with a value of 1 signifying the absence of association, the odds ratio is not optimal for visualization in our network; therefore, we used the natural logarithm of the odds ratio. A log odds ratio of 0 (i.e., an odds ratio of 1) indicates that the event is equally likely in both groups. Please note that a high co-occurrence ($= n_{11}$) does not necessarily imply a high odds ratio. For example, (1) a high co-occurrence ($n_{11} = 500$), (2) almost no people who do not have both symptoms ($n_{22} = 3$), and (3) thus, relatively many people who have one or the other symptom ($n_{12} = 15$ and $n_{21} = 100$) yields an odds ratio of 1 (500*3/100*15), signaling no association between those symptoms. Thus, co-occurrences and odds ratios show different aspects of a data set.

6. In fact, we also computed tetrachoric correlations for the MDD and GAD symptoms with a full information maximum likelihood approach through which we dealt with the missing values that were Missing At Random (MAR). We found that the ordering of the symptoms in terms of their node strength was nearly the same as with log odds ratios.

7. We have checked the stability of the results depicted in this figure by randomly splitting the sample in two and running all analyses for both groups separately. Those separate analyses revealed the same results and, therefore, we consider the components of Figure 4 to be stable.

8. The fact that duration is weakly associated with the other MDD and GAD symptoms cannot be explained by a skip structure that only allowed respondents to progress to the other symptoms' section if they fulfilled the duration criteria for depressed mood/loss of interest (MDD: more than 2 weeks) and chronic anxiety (GAD: more than 6 months): respondents with depressed mood/loss of interest for at least 3 days for more than 1 hour per day (MDD) as well as respondents with chronic anxiety for at least 1 month were allowed into the sections about the other symptoms.

9. It is important to note here that within a latent variable framework, factor loadings cannot be measures of symptom centrality as we view the concept, since those loadings are simply reliability estimates: the higher the factor loading, the more reliably an indicator "represents" the common cause.

10. The contingency tables, as well as the computational script (made in R), are available at: http://www.aojcramer.com. We have checked the stability of the results depicted in Figure 6 by randomly splitting the sample in two and have run all analyses for both groups separately. Those separate analyses revealed the same results, and therefore, we consider the components of Figure 6 to be stable.

Open Peer Commentary

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doi:10.1017/S0140525X10000580

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Abstract: We discuss the latent variables construct, particularly in regard to the following: that latent variables are considered as the sole explanatory factor of a disorder; that pragmatic concerns are ignored; and that the relationship of these variables to biological markers is not addressed. Further, we comment on the relationship between bridge symptoms and causality, and discuss the proposal in relationship to other constructs (endophenotypes, connectionist-inspired networks).

Since the early stages of the discipline of psychiatry, the construct of psychiatric semiology and nosography has been indissociable from the etiological conceptualization of observed phenomena. Nevertheless, it is widely admitted that psychiatric disorders are multifactorial and etiologically complex, and explanatory models should refer mostly to *explanatory pluralism* rather than to *biological reductionism*. Our knowledge about psychiatric disorders remains incomplete, and we can only hope to get "small explanations, from a variety of explanatory perspectives, each addressing part of the complex etiological process leading to disorder," and try to understand "how these many different small explanations all fit together," etiological pathways being considered "complex and interacting more like networks than individual pathways" (Kendler 2005, p. 435). Our current categorical classifications of mental disorders in the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (*DSM-IV*; American Psychological Association 1994) and in the World Health Organization's International Statistical Classification of Diseases, 10th revision (*ICD-10*) have been conceptualized on assumptions of more global and simple hypothetical explanations.

In that context, the clinical assessment of psychiatric conditions has been addressed in reference to the "latent trait hypothesis," which considers each observed symptom or cluster of symptoms to be related to a specific latent cause.

Any attempt to go beyond the usual categorical construct of current mental disorders classifications could constitute a valuable epistemological contribution in view of the upcoming new version of mental disorders classifications (*DSM-V*), as it takes an important step toward a less categorical, and rather dimensional conception of mental disorders. We have the following specific comments to make on Cramer et al.'s discussion of latent variables in the target article.

1. The target article makes a restrictive interpretation of the *latent variable models*. Along the article's lines, latent variable models are represented as *unidirectional* trees, the "latent variable" (the common cause) being the root. In this representation, the authors assume that all links have the same importance. Yet, by definition, a latent variable is only non-observable, and is not necessarily causally central. Cramer et al. are probably right in criticizing the assumption (implicit in psychiatry) that all symptoms should be related to a *central* latent variable, but they mistakenly underestimate the potential role of *accessory* latent variables. Getting rid of all latent variables would be tantamount to assuming that everything is known about the observed phenomenon. Moreover, there is no reason why the flexibility they claim for their network approach (multi-directionality, different link strength) should not be allowed within the context of a latent variable model.

2. Besides, a heuristically good reason to suppose the existence of a latent variable is mainly therapeutic rather than methodological. This kind of hidden variable is often seen as a therapeutic target rather than an etiological node; that is, not something to find that would explain everything, but something to act upon that would dissolve everything. If a match is considered *the* cause of a fire in a building, rather than oxygen in the air, which is no less required to start a fire, it is because the match seems the most appropriate factor to act upon. Mackie (1974), Hesslow (1984), Gannett (1999), and Magnus (1992), among others, have shown the importance of pragmatic concerns in the search for a single target which might be called *the* cause of a disease (it is called the problem of *causal selection*). This kind of pragmatic interpretation of a latent variable as "what we have to act upon" may justify the otherwise objectionable assumption that there is actually a latent variable which explains and causes everything. There is, however, a question as to how the network approach is to be translated into the definition of therapeutic targets. For instance, while such a definition is obviously easy on the basis of the target article's Figure 1, one might ask what could be proposed on the basis of Figure 4.

3. It would also be interesting to discuss this model, as well as the latent variable model, with regard to the biological markers of these diseases. Indeed, particular markers of the disorder could be related to specific biological alterations. For example, anhedonia could be related to a deficit in nucleus accumbens processing, or a defect in stress reactivity to a dysregulated neuroendocrine axis.

4. Beyond that, in the case of two comorbid disorders, do the authors propose that each symptomatic node be related to a specific biological dysfunction that would be common to the two comorbid pathologies? In this case, a given biological marker defect underlying pathology A would also be altered in the comorbid pathology B. If there is no latent variable underlying the different symptomatic features, what is the explanation as to why these symptoms often co-occur? Moreover, if two comorbid disorders have a common epiphenomenal symptom, should this be regarded as a *bridge symptom*? For example, if decreased eating occurs in an anxiety disorder as well as in depression, but does not induce (or is unrelated to) any of the other symptoms of depression or anxiety, might it not be considered a bridge symptom underlying comorbidity? How can symptoms be distinguished from "non-symptom causal processes" (sect. 2, para. 9) or from the "external effects" (sect. 5, para. 6) if the boundaries of the disorders are "fuzzy" (sect. 6, para. 6)?

5. It would be interesting to compare the network model described by Cramer et al. with the psychopathological endophenotype approach that has been developed to dissect major depression into different independent entities (see, e.g., Hasler et al. 2004), or with other constructs used in the field of psychiatry, such as connectionist-inspired ones (e.g., Tanti & Belzung 2010).

The rocky road from Axis I to Axis II: Extending the network model of diagnostic comorbidity to personality pathology

doi:10.1017/S0140525X10000592

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Abstract: Although the network model represents a promising new approach to conceptualizing comorbidity in psychiatric diagnosis, the model applies most directly to Axis I symptom disorders; the degree to which the model generalizes to Axis II disorders remains open to question. This commentary addresses that issue, discussing opportunities and challenges in applying the network model to *DSM*-diagnosed personality pathology.

Cramer et al.'s network model represents a promising new approach for conceptualizing and quantifying comorbidity in psychiatric diagnosis, helping avoid the thorny challenge of operationalizing latent constructs, and shifting the focus of comorbidity research from syndrome to symptom. Scrutiny of Cramer et al.'s analysis reveals that the theoretical underpinnings and empirical evidence bearing on this model apply most directly to Axis I symptom disorders (e.g., major depression, generalized anxiety). Because Axis II personality disorders differ in myriad ways from Axis I symptom disorders, the degree to which the network comorbidity model generalizes to Axis II disorders remains open to question. This commentary addresses that issue, discussing issues that arise in applying the network model to *DSM*-diagnosed personality pathology (i.e., the personality disorder [PD] diagnoses offered in the *Diagnostic and Statistical Manual of Mental Disorders, 4th edition* or *DSM-IV*; American Psychiatric Association 1994).

As Cramer et al. have noted, diagnostic comorbidity evidence involving *DSM-IV* Axis I disorders can yield ambiguous, confusing patterns. Diagnostic comorbidity evidence bearing on *DSM-IV* Axis II is far worse. Consider: The number of differential diagnoses per *DSM-IV* PD ranges from 3 (dependent, obsessive-compulsive) to 7 (paranoid), with the mean number of differential diagnoses per PD being 4.5. Thus, on average each *DSM-IV* PD shows substantial overlap with 50% of the remaining PDs. When Ekselius et al. (1994) calculated correlations among interview-derived scores for PDs in a heterogeneous sample of psychiatric patients and nonclinical participants, they obtained a mean interscale correlation (r) of .41, and statistically significant interscale correlations in 41 of 45 comparisons (91%). Subsequent comorbidity studies have confirmed these results (Bornstein 1998; 2005).

Given these patterns, extending the network comorbidity model to Axis II presents some unique challenges, but it also involves some unique opportunities to gain new perspective on