A Network Perspective on Comorbid Depression in Adolescents with Obsessive-compulsive Disorder

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Abstract

People with obsessive-compulsive disorder [OCD] frequently suffer from depression, a comorbidity associated with greater symptom severity and suicide risk. We examined the associations between OCD and depression symptoms in 87 adolescents with primary OCD. We computed an association network, a graphical LASSO, and a directed acyclic graph (DAG) to model symptom interactions. Models showed OCD and depression as separate syndromes linked by bridge symptoms. Bridges between the two disorders emerged between obsessional problems in the OCD syndrome, and guilt, concentration problems, and sadness in the depression syndrome. A directed network indicated that OCD symptoms directionally precede depression symptoms. Concentration impairment emerged as a highly central node that may be distinctive to adolescents. We conclude that the network approach to mental disorders provides a new way to understand the etiology and maintenance of comorbid OCD-depression. Network analysis can improve research and treatment of mental disorder comorbidities by generating hypotheses concerning potential causal symptom structures and by identifying symptoms that may bridge disorders.

Keywords: Obsessive-compulsive disorder, depression, network analysis, comorbidity, adolescent psychopathology

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Obsessive-compulsive disorder (OCD) is a debilitating and persistent syndrome that affects both youth and adults. It is characterized by repetitive intrusive thoughts and urges, and accompanied by compulsive thoughts and actions designed to relieve the distress caused by these obsessions (American Psychiatric Association, 2013). Depression is a common comorbidity in patients with OCD, with lifetime rates estimated at 62.7-78.2% (Pinto, Mancebo, Eisen, Pagano, & Rasmussen, 2006; Millet et al., 2004). Depression tends to follow, rather than precede OCD (Ricciardi & McNally, 1995), especially among those with early-onset OCD (Millet et al., 2004). OCD is associated with reduced quality of life and deficits in psychosocial functioning, which are risk factors for depression (Eisen et al., 2006). Depression does not usually impede treatment outcomes for OCD (Olatunji, Davis, Powers, & Smits, 2013), although severe depression sometimes does (Foa, 1979). The elevated risk of suicide attempts (Torres et al., 2011; Kamath, Reddy, & Kandavel, 2007) and increased OCD symptom severity (Brown, Lester, Jassi, Heyman, & Krebs, 2015) among those with comorbid depression are more worrisome.

Although OCD in children and adolescents is broadly similar to adult OCD, it has several distinctive features. Pediatric OCD is more common among boys than girls, whereas adult OCD is more common among women than men (Shafran, 2001; Karno, Golding, Sorenson, & Burnam, 1988). Comorbid depression is more common in adults and adolescents (78% & 62%, respectively) than in children (39%; Geller et al., 2001), whereas comorbid Tourette's disorder is more common in children (25%) than adolescents (9%) or adults (6%; Geller et al., 2001). Those with early onset cases of OCD had lower rates of lifetime comorbid depression (73.4%) than those with late onset OCD (81.2%; Millet et al., 2004). Comorbid disruptive disorders such as oppositional defiant disorder and ADHD are more common in youth than adults (Geller et al., 2001; Hanna, 1995).

The emerging network theory of mental disorders provides a new way to understand psychopathology. It differs from traditional categorical and dimensional models that presuppose an underlying disease entity as the common cause of symptom emergence and covariance (Borsboom & Cramer, 2013; Cramer, Waldorp, van der Maas, & Borsboom, 2010). The latent categorical (or dimensional) disease model accurately characterizes many nonpsychiatric medical disorders: consider, for instance, rhinovirus infection (the common cold). Imagine someone with a cold who has both a dry throat and a runny nose. In the disease model, the dry throat and runny nose occur together, but they do not cause one another. They are both caused by a third variable: the disease. In other words, the dry throat and runny nose are locally independent; they share a common cause, but do not influence one another in a causal fashion (Borsboom, Mellenbergh, & van Heerden, 2003).

Unfortunately, categorical and dimensional models have seen limited success in illuminating the mechanisms of mental disorders. This has led some to hypothesize that the long-searched-for latent causes might not exist (Borsboom & Cramer, 2013; McNally, 2016). If latent causes of mental disorders do not exist, how do symptoms arise, and why do they frequently covary? The network theory of mental disorders asserts that symptoms of mental disorders are *causing each other* in feedback loops that settle into self-sustaining equilibria (Borsboom & Cramer, 2013; McNally, 2016). In this view, having a mental disorder means having harmful symptom patterns that persist after external triggers have abated (e.g., hysteresis; Cramer et al., 2016).

The network theory conceptualizes symptoms of mental disorders as *constitutive* of the disorder, rather than reflective of an underlying disease entity. Networks depict the components of a system (nodes) and the links between each of these components (edges). In psychopathology networks, nodes generally correspond to symptoms (Borsboom, in press). Modeling symptom associations can help illuminate the etiology and maintenance of mental disorders.

Consider a hypothetical network model of depression in a fictional patient named John. Relationship difficulties make John feel sad and guilty. His sadness and guilt cause insomnia, and the following morning he feels exhausted with impaired concentration. These symptoms make him feel more worried and sad, which cycles back by causing greater insomnia the next day. After several weeks of constant symptoms, John sees a professional and is diagnosed with clinical depression. What caused and maintained John's depression? No underlying disease was involved. Rather, an external event (relationship difficulties) activated symptoms in the network (sadness and guilt), which created a looping chain of additional, related symptoms.

When the symptoms between two different disorders are linked, having one disorder can activate another disorder. Identifying *bridge symptoms* can illuminate how comorbidities develop and help us understand why comorbidities occur in some individuals but not in others. For instance, if we suppose that guilt is a bridge symptom between OCD and depression, then a patient who feels guilty about his or her OCD symptoms would be at greater risk for depression compared to a patient with equally severe OCD, but who did not feel especially guilty. It would therefore be wise for clinicians to target these bridge symptoms therapeutically to thwart the emergence of comorbidity.

It is unclear why OCD and its comorbidities manifest differently depending on age. McNally et al. (2016) examined OCD and depression symptoms in 408 adult patients with primary OCD. Their analysis revealed that sadness, anhedonia and obsession-related distress were the symptoms with the highest level of connections to other symptoms. Their model also predicted that OCD symptoms lead to depression symptoms when obsessional distress leads to sadness.

In the present study, we used network analysis to explore the possible functional relations among OCD and depression symptoms in adolescents about to undergo treatment for OCD. We had two chief aims. Our first aim was to further develop the network model of OCD-depression comorbidity. Our

second aim was to examine the distinctions that emerge between the adolescent network of OCD-depression comorbidity and the adult network in McNally et al. (2016).

Methods

Participants

The participants were 87 adolescents beginning treatment for OCD in the residential and intensive outpatient units of the Obsessive-Compulsive Disorder Center at Rogers Memorial Hospital. There were 41 (47.1%) males and 46 (52.9%) females, who ranged in age from 13 to 17 (M = 15.37, SD = 1.17). The racial/ethnic breakdown was Caucasian (n = 72), Asian (n = 10), Hispanic (n = 2), biracial (n = 2), and Black (n = 1). All participants received a primary diagnosis of OCD upon enrollment, and each consented for their data to be used in de-identified research. Comorbid disorders were major depression (24.1%), depressive mood disorder not otherwise specified (47.1%, combined percentage = 71.3%), attention deficit hyperactivity disorder (28.7%), generalized anxiety disorder (20.7%), social anxiety disorder (11.5%), and tic/Tourette's syndrome (9.2%). A staff psychiatrist used DSM-IV criteria to diagnose patients.

Measures

Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS; Scahill et al., 1997). The CY-BOCS is a self-report questionnaire that evaluates the severity of OCD symptoms during the previous week. The scale includes 10 five-point Likert items which are summed to a score that ranges from 0-40 (a score of 16 or above signifies clinically significant severity). Reliability and validity of the self-report version of the scale are satisfactory (Scahill et al., 1997). The mean score in our sample was 26.1 (SD = 5.8, range = 24). The 10 questions in the CY-BOCS correspond to the 10 questions in the adult version of the scale (Y-BOCS; Goodman et al., 1989). For our figures, we used the following abbreviations for CY-BOCS symptoms: 1) *obtime* (time occupied by obsessive thoughts), 2) *obinterfer*

(interference in one's life due to obsessive thoughts), 3) *obdistress* (distress associated with obsessive thoughts), 4) *obresist* (difficulty resisting obsessions), 5) *obcontrol* (difficulty controlling obsessions), 6) *comptime* (time spent performing compulsive behaviors), 7) *compinterf* (interference in one's life due to compulsive behaviors), 8) *compdis* (distress associated with compulsive behavior), 9) *compresis* (difficulty resisting compulsions), and 10) *compcont* (difficulty controlling compulsions).

Quick Inventory of Depressive Symptomatology (QIDS-SR; Rush et al., 2003). The QIDS-SR is a self-report questionnaire that evaluates the severity of depression symptoms. The scale includes 16 four-point Likert items summing to a total score ranging from 0-64. Reliability and validity of the scale are satisfactory (Rush et al., 2003). The mean score in our sample was 10.7 (SD = 5.9, range = 25). For our figures, we used the following abbreviations for QIDS symptoms: 1) *onset* (difficulty falling asleep), 2) *middle* (sleep during the night), 3) *late* (waking up too early), 4) *hypersom* (sleeping too much), 5) *sad* (feeling sad), 6) *decappetite* (decreased appetite), 7) *incappetite* (increased appetite), 8) *weightloss* (decreased weight within the last two weeks), 9) *weightgain* (increased weight within the last two weeks), 10) *concen* (impairment in concentration/decision making]), 11) *guilt* (self-blaming view of oneself), 12) *suicide* (thoughts of death or suicide), 13) *anhedonia* (loss of general interest), 14) *fatigue* (low energy level), 15) *retard* (feeling slowed down), and 16) *agitation* (feeling restless).

Analyses

Association network and community analysis. Using the R package *qgraph* (R Core Team, 2016; Schmittmann & Borsboom, 2013) we computed an association network that depicts Pearson product-moment correlations between pairs of nodes. Only the strongest correlations appear in the graph ($r > |.25|$). The resultant network is a graphical depiction of a correlation matrix.

We then conducted analyses to test for communities of nodes in this network. Communities are clusters of nodes whose interconnections are especially dense. In psychopathology networks,

communities often correspond to syndromic subnetworks within the larger network (e.g., cluster of grief symptoms versus a cluster of depression symptoms; Robinaugh, LeBlanc, Vuletich, & McNally, 2014). Community analysis is a mathematical approach to identifying subnetworks within a larger network structure (Fortunato, 2010).

Our intention in using community analysis was to determine whether OCD and depression could be reliably detected as separate communities. We used the spin-glass community detection method, as was most appropriate given our network, as well as four additional methods to ensure the stability of the community structure across methodologies. We used the follwing functions from the R package *igraph* (Csardi & Nepusz, 2006) to detect communities: spin-glass (*spinglass.community*), walk-trap (*walktrap.community*), leading eigenvector (*cluster_leading_eigen*), edge-betweenness (*cluster_edge_betweenness*), and fast-greedy (*cluster_fast_greedy*).

Graphical LASSO. We generated a graphical LASSO (Least Absolute Shrinkage and Selection Operator) model (Friedman, Hastie, & Tibshirani, 2011) using the Extended Bayesian Information Criterion function *EBICglasso* in the R package *qgraph* (Schmittmann & Borsboom, 2013). The graphical LASSO depicts regularized partial correlations between pairs of symptoms, retaining only the largest, potentially causal ones. The LASSO applies an L1 penalty that shrinks trivially small partial correlations to zero and thus removes such likely spurious edges from the network. The severity of the sparsity parameter can be adjusted between 0 and 1; given our small sample size, we set the tuning parameter to 0.3 (a relatively low stringency) to attempt a balance between sparseness and sensitivity. The resultant network graphically depicts a partial correlation matrix with trivally small associations removed.

Directed acyclic graph (DAG). The DAG is a graphing procedure based in Bayesian mathematics that gives us information about both the strength and the *direction* of connections.

Directions give us clues as to what symptom associations might be causally important. The DAG models a network in which edges are *directed* and *noncircular*. Directed edges allow us to determine preliminary hints as to which symptoms play a causal role in creating other symptoms.

We modeled the DAG by bootstrapping the Bayesian hill-climbing function *hc* in the R package *bnlearn* (Scutari, 2010) and creating an average of the 1,000 bootstrapped networks. The hill-climbing algorithm functions by repeatedly creating new models of the network, and testing these models by their goodness-of-fit to the observed data. We verified the network stability by accepting only the edges that appeared in a large proportion of the models, based on the optimal significance threshold for inclusion (Scutari & Nagarajan, 2013).

Centrality. In addition to generating the networks, we computed metrics for measuring centrality of nodes in each network. Centrality in a network refers to the degree to which a given node is important to the rest of the network. The centrality of nodes in a psychopathology network indicates which symptoms are theoretically playing a key role inmaintaining the disorder. We computed *strength centrality, betweenness centrality,* and *closeness centrality*. Strength centrality is the sum of all the weights connected to a given node. In other words, strength centrality measures a node's total correlation with all other nodes. Betweenness is the number of times that a node lies on the shortest path between two other nodes, and closeness is the average length of the shortest path between the given node and all other nodes in the network.

Results

Association Network

Figure 1 presents the association network. Weight loss and decreased appetite (*weightloss*, *decappetite*) were isolated, with no strong edges ($r > |0.25|$) connecting to the rest of the network. Hypersomnia, weight gain, and increased appetite (*hypersom*, *weightgain*, *incappetite*) were weakly

connected to the rest of the network. Two important bridges between OCD and depression symptoms emerged: distress associated with obsessions (*obdistress*) linked to concentration difficulties, sadness, and guilt (*concen*, *sad*, *guilt*), and lack of control over obsessions (*obcontrol*) linked to guilt (*guilt*). Concentration problems (*concen*) emerged as the most central node in the network in terms of betweenness, closeness, and strength centrality. Other notable high centrality nodes included sadness, time spent obsessing, and distress associated with obsessions (*sad*, *obtime*, *obdistress*). Normalized centrality metrics appear in the supplemental materials.

Community analysis mathematically detects subgroups within a network. We used several community detection algorithms (see Table 1). Analyses were confirmatory of visual interpretation: depressive symptoms and OCD symptoms formed two separate communities in each analysis, with weight and sleep-related symptoms most commonly diverging from this basic structure.

Graphical LASSO

The graphical LASSO starts with partial correlations, and then applies a penalty to small correlations, shrinking them to zero and resulting in a sparser network that represents only the largest edges (Figure 2). Edges appearing in the association network that remain in the graphical LASSO are those most likely to constitute genuine causal connections. Node centrality metrics of the graphical LASSO are presented in Figure 3. Concentration impairment (*concen*) remained as the most central node in the network in terms of betweenness, closeness, and strength, with time spent with obsessions, sadness, and fatigue (*obtime*, *sad*, *fatigue*) as other notably central nodes.

Bayesian Directed Network (Directed Acyclic Graph [DAG])

Figure 4 presents the DAG. The directed nature of the DAG provides clues about causality, which can guide future research. The clues we gain from the DAG can give us a good idea of what to investigate in future time-series or experimental procedures. However, a common misinterpretation must

be avoided: direction alone cannot be interpreted as a causal effect. The DAG is used here for hypothesis *generating*, rather than hypothesis *testing*. The hill-climbing algorithm creates random models which include direction of prediction and then iterates until a goodness-of-fit score is achieved. This direction does not imply temporal precedence, and thus gives limited information about causation. In other words, the DAG assumes a causal story (unidirectional, non-looping predictions), and finds the best possible model to fit the given data with that story. It does not confirm causation, it simply tells us what structure our data would take if causation were present.

In our averaged model, OCD symptoms predicted depression symptoms. This direction of prediction is consistent with the literature on OCD and depression comorbidity (Ricciardi & McNally, 1995; Millet et al., 2004) as well as the directed model presented in McNally et al. (2016). The actual nodes involved, however, departed from the aforementioned adult model: the main connections between OCD and depression related symptoms were from *obtime* to *concen* and from *obcontrol* to *guilt*. In adults, the connection between OCD and depression related symptoms was from *obdistress* to *sad*.

Discussion

We used network analysis to model pediatric OCD-depression comorbidity as a system of inter-symptom functional relations. In our analysis, OCD symptoms and depression symptoms reliably clustered into two separate communities. This provides support for the conceptualization of OCD and depression as distinct, yet related, syndromes. Our approach assumes that these syndromes exist as communities of interacting symptoms rather than categorical disease entities.

Network theory may be particularly helpful for comorbidities: if we focus prevention and treatment on the symptoms that link two comorbid disorders, we may be able to reduce comorbidities by effectively "burning the bridge". The bridge symptoms that linked the two communities in our exploratory networks were obsessional problems in the OCD community (*obdistress, obcontrol, obtime*)

and concentration difficulties, guilt, and sadness in the depression community (*concen, guilt, sad*). In the DAG, OCD symptoms predicted depression symptoms, and not the reverse. This is convergent with research that suggests that OCD generally precedes depression when the two are comorbid (Millet et al., 2004; McNally et al., 2016). Moreover, the connection between OCD and depression emerged through the obsessional branch of the network, not the compulsive one. This converges with evidence that depressed mood (Ricciardi & McNally, 1995) and severity of comorbid major depression (Besiroglu, Uguz, Saglam, Agargun, & Cilli, 2007) are related to obsessions, but not to compulsions.

Guilt was a bridge symptom linking the OCD community to the depression community. Guilt is a common feature of both syndromes: state and trait guilt are elevated in sufferers of OCD (Shafran, Watkins, & Charman, 1996), and are linked to depressive symptoms (Kim, Thibodeau, & Jorgensen, 2011). Additionally, guilt is a common focus of obsessions; some suggest that pathological guilt is a core feature of OCD (Shapiro & Stewart, 2011). Guilt is implicated in the relationship between social anxiety disorder and depression (Heeren & McNally, 2016; Hedman, Ström, Stünkel, & Mörtberg, 2013), and is a prominent feature in general anxiety disorder (Fergus, Valentiner, McGrath, & Jencius, 2010) and PTSD (Lee, Scragg, & Turner, 2001), suggesting that guilt may be a transdiagnostic feature that links a multitude of mental disorders. Our exploratory model suggests the hypothesis that adolescent sufferers of OCD with high levels of guilt may be at elevated risk of developing comorbid depression.

Impairment in concentration and decision-making (*concen*) was the most central node and a bridge between OCD and depression. This finding is of special interest given that this node was relatively less important in the adult network (McNally et al., 2016). Concentration impairments may be more salient in the functional context of the adolescent world. Piacentini, Bergman, Kellser, & McCraken (2003) reported that the two most common functional problems in pediatric OCD were 1) problems concentrating on schoolwork and 2) doing homework. This illustrates the potential importance

of life-context in a network conceptualization of mental illness, as well as the importance of tailoring networks to the group of interest.

Centrality was low for the sleep and appetite-related symptoms of depression. These symptoms also diverged from the general structure of depression and OCD in the community analysis. This suggests that the somatic symptoms included on the QIDS are not central in a network conceptualization of depression. This finding converges with evidence that points to the general heterogeneity of depression symptoms (Fried & Nesse, 2015) and improvements in homogeneity in depression assessments that focus on the core symptoms of depression (Lecrubier & Bech, 2007). This finding also demonstrates the potential utility of network analysis in clinical treatment: according to our model, it is highly unlikely that treatment focusing on controlling these symptoms would have much impact on the remaining symptoms of OCD and depression.

The network approach to psychopathology opens doors to exploring the potential mechanisms involved in the etiology and maintenance of mental disorders. Networks provide us with a view of how symptoms are interrelated. Considering the difficulty of classifying overlapping comorbidities in a latent model view, network analysis offers a refreshing approach that explains the overlap between syndromes with clarity. Most importantly, network structures could potentially inform interventions to have the most impact in preventing and treating disorders and their comorbidities.

Limitations

The ramifications of our analysis are notable. However, our method comes with several limitations. First, our sample size was relatively small considering the high statistical power necessary in network analysis; a small sample size can lead to instability in the LASSO and DAG. An analysis on network stability showed the LASSO to be acceptably stable, with some limitations (see supplemental

materials). The values presented in the DAG are a result of the average of 1,000 of bootstrapped models. Bootstrapped samples for the DAG also showed acceptable stability.

Our methods were exploratory, not experimental. Accordingly, the main implications for clinical practice should be an awareness of likely "central symptoms" and "bridge symptoms" in OCD and depression. If the edges emanating from bridge symptoms and high-centrality symptoms are causal, then the therapeutic resolution of these symptoms should hasten recovery faster than should successful treatment of less important symptoms. A full understanding of symptom interactions can only be achieved by a fully causal model. Although approaches such as the graphical LASSO and DAG can move cross-sectional data *closer* towards a causal interpretation (McNally et al., 2016), networks derived from cross-sectional data are limited by definition. All three networks are observational and exploratory rather than experimental. Although we believe that network approaches to cross-sectional data can yield some preliminary causal clues, experimental data remain the gold standard for establishing causal claims. In addition, correlational approaches (association network, graphical LASSO) are limited because they cannot model direction, and the DAG is limited because it cannot model cyclicity. Results are therefore best interpreted through the convergence of several methods, in conjunction with evidence from the literature.

Future studies could improve upon our approach by measuring the change in symptoms over time and by including experimental manipulations. Time-series data allows for modeling networks that are both directed and cyclic. Using time-series data also creates the capability of generating networks on an individual level. Because relationships between symptoms that appear at the inter-individual level may vary between individuals, creating individual networks would be useful to help clinicians laser in on only the most central nodes in a particular patient's network of symptoms. Experimental

manipulations such as clinical interventions aimed at specific nodes could test for causality within the network.

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Figure 1. Association Network.

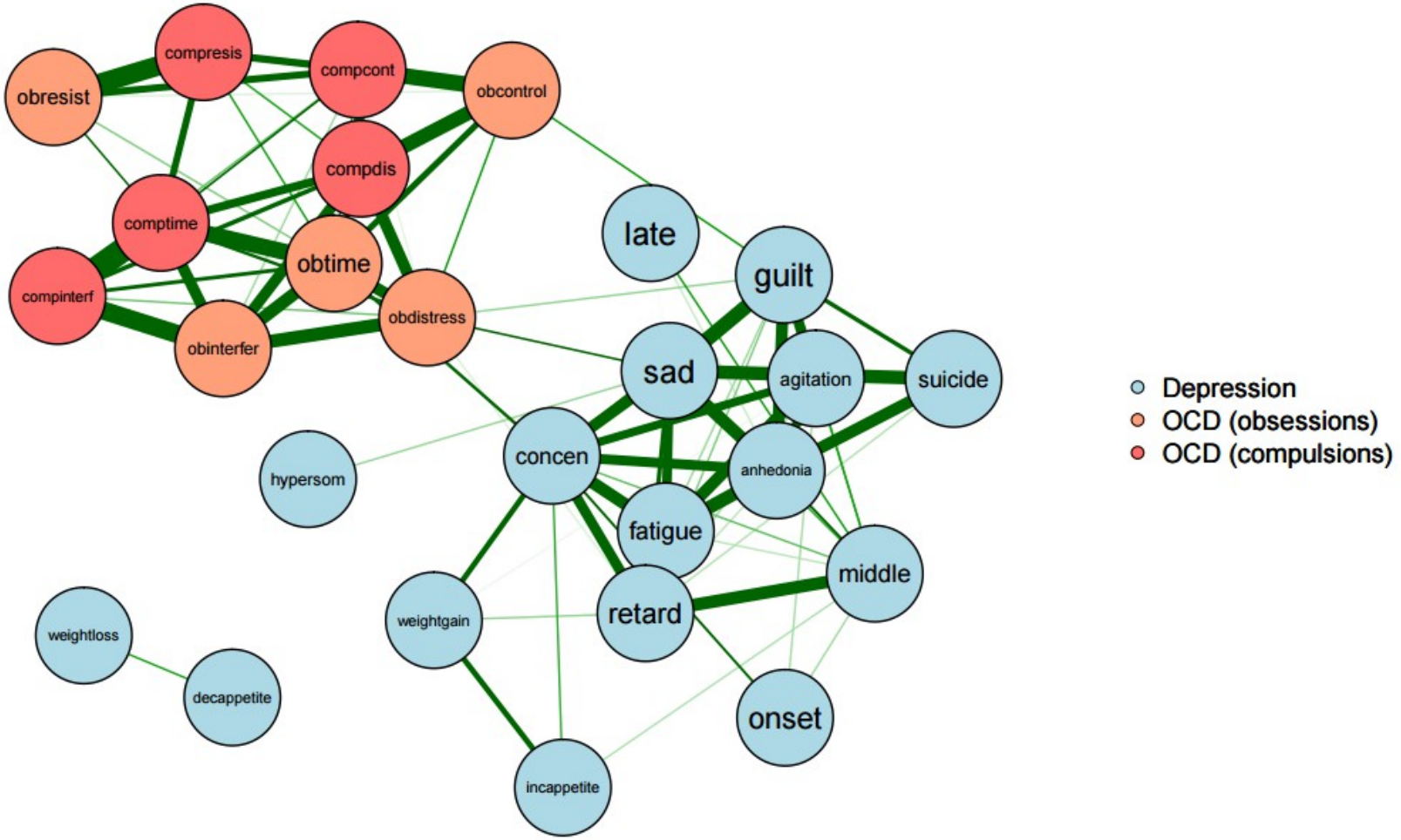

Figure 2. Graphical LASSO.

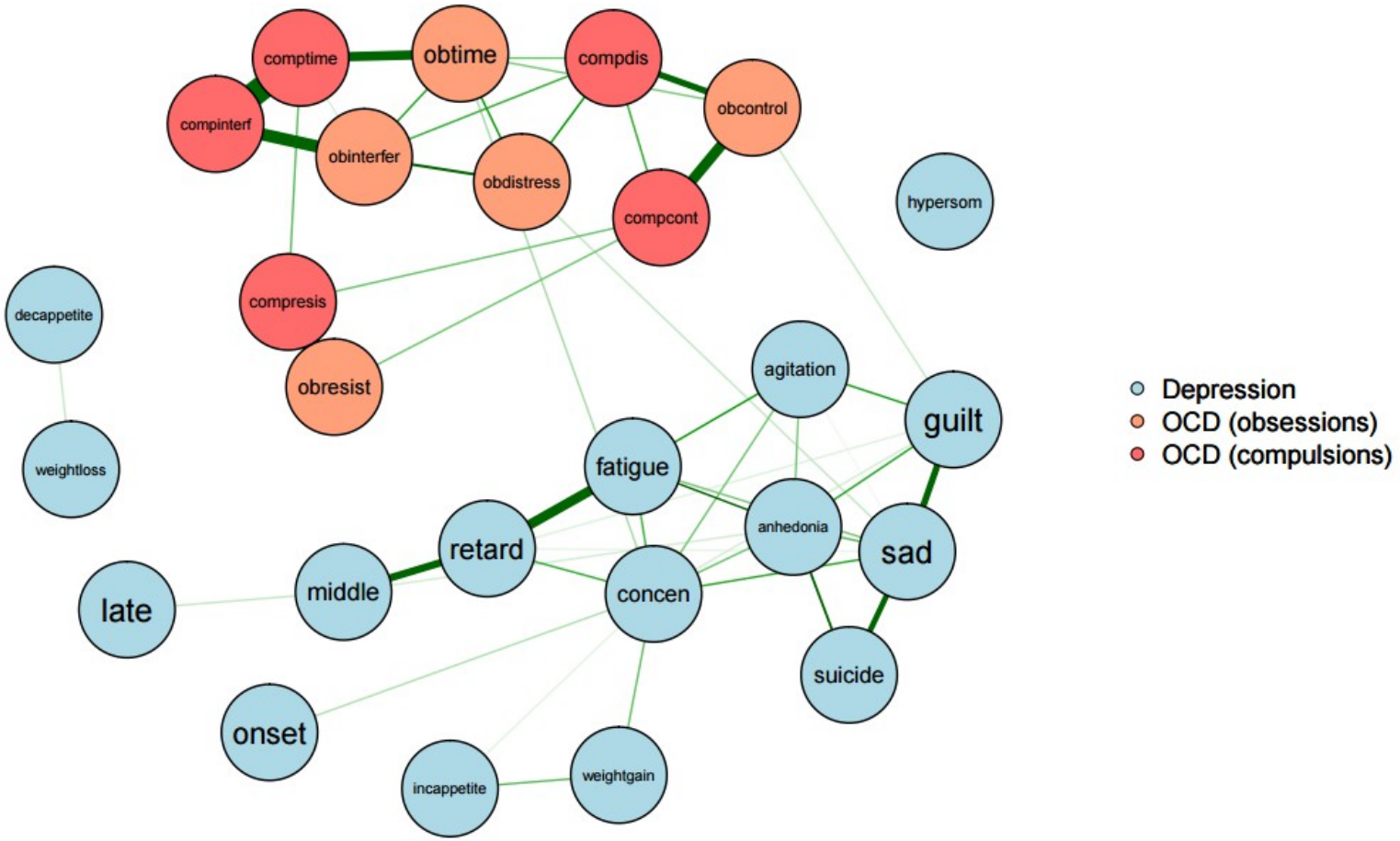

Figure 3. Graphical LASSO Centrality.

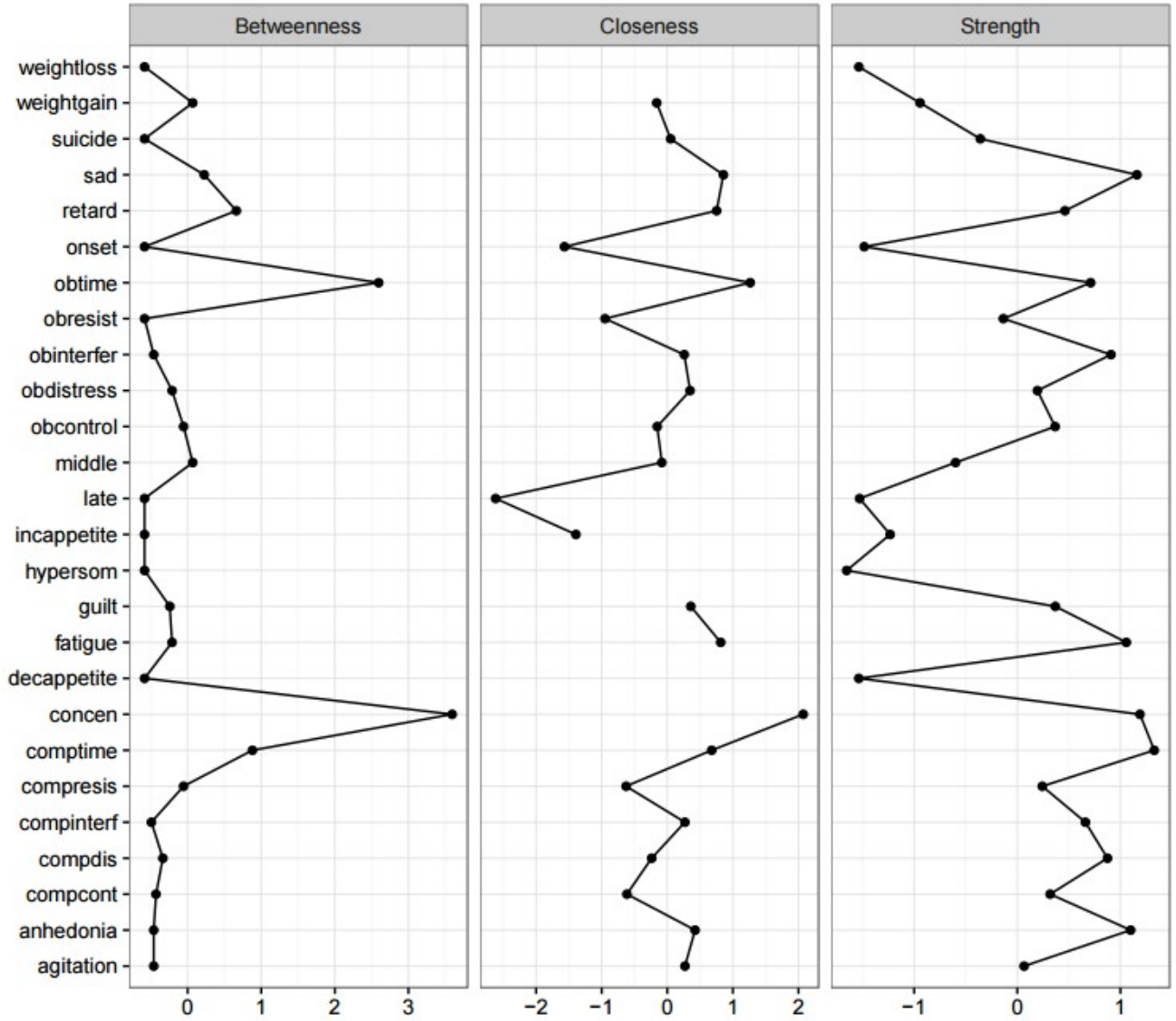

Figure 4. Directed Acyclic Graph